HIDRADENITIS SUPPURATIVA

WYN P. MORGAN

SUBMITTED IN CANDIDATURE FOR

THE DEGREE OF Ch.M.

UNIVERSITY OF EDINBURGH

1985

ABSTRACT OF THESIS (Regulation 6.9)

Name of Candidate WYN P. MORGAN

Address .....

Degree Ch.M. *Date* 24th APRIL 1985.

Title of Thesis HIDRADENITIS SUPPURATIVA.

The work described is based upon 75 patients with active chronic hidradenitis suppurativa.

Previous work suggests that hidradenitis is due to an abnormality of the apocrine sweat glands. The possibility that the size or number of the apocrine glands in hidradenitis may differ from normal has not been previously investigated. This study shows that no such difference exists but that the axillary apocrine glands are larger in hyperhidrosis.

The detailed distributions of the apocrine glands in the axilla and pubo-inguino-perineal area have been demonstrated for the first time. This was achieved by the development of the atropine/iodine/starch and oxytocin method of producing and detecting apocrine sweating; the results were confirmed by microscopy of the excised skin. Apocrine glands were abundant in the axilla but were sparsely distributed in the pubo-inguino-perineal area.

The surgical treatment given was based upon the proposition that excision of the apocrine gland concentrations in the diseased area was necessary to ablate hidradenitis. This was successful in the axilla but less successful in the pubo-inguino-perineal area with recurrence rates of 1% and 24% at median follow up of 39 and 43 months respectively.

Healing by granulation of the axillary defects was compared with split skin grafting. Full limb mobility without wound contracture was obtained by both methods. Grafting, when successful, resulted in faster healing, but healing by granulation was certain and gave a better cosmetic result. Healing by granulation in the pubo-inguino-perineal area was efficient and achieved good cosmesis.

Hidradenitis was more common in females than males; its maximum incidence occurring in the second and third decades of life. The most commonly involved site was the axilla followed by the pubo-inguinal area. It is associated with acne vulgaris and epidermoid cysts, suggesting that it is a disease of the pilo-sebaceous unit. Hidradenitis patients have an increased prevalence of a positive family history of hidradenitis, which may result from common genetic or environmental factors. Exacerbations of hidradenitis with menstrual periods and remissions during pregnancy can occur. The disease is not associated with diabetes mellitus and the use of deodorants, depilatory agents, and mechanical shaving are not primary aetiological factors.

ACKNOWLEDGMENTS

The work reported in this thesis is the result of my research carried out as a research registrar at the Department of Surgery, of the University Hospital of Wales, Cardiff. I have pleasure in recording my gratitude to Professor L. E. Hughes who provided me with research facilities in his department and for his advice, support and encouragement during the project.

I should also like to thank Mrs. Glenys Elliott for her technical assistance in preparing the histological slides, and Professor Marks of the Department of Dermatology, of the University Hospital of Wales, Cardiff, for making the use of the Quantimet 70 available to me.

The clinical, histological and surgical studies were personally performed. I am grateful to Dr. Craigmyle of the Department of Anatomy, University College, Cardiff for his helpful advice in regard to the apocrine sweat glands and for the provision of cadaveric skin specimens.

I am grateful to Dr. R. Newcombe of the Department of Medical Statistics who provided invaluable advice in the gathering and analysis of patient data.

The photographic record of the lesions, specimens and surgery was essential to the project and I am grateful to Dr. R. Marshall and the Department of Medical Illustration of the University Hospital of Wales, Cardiff for their enthusiastic co-operation.

I am grateful to Mrs. Marjorie Barker for her patience and tolerance in the typing of the text and tables. Mr. D. Grimshaw prepared the illustrations.

The provision of technical assistance for the preparation of histological slides was funded by a Medical Research Council grant.

Finally I should like to thank the Consultant Surgeons and Dermatologists of the Cardiff Hospitals for their interest in the project.

DECLARATION

This thesis has been composed by myself and the work described therein reflects my own research.

Date: 1/5/85 Signature: Wyn P. Morgan.

PUBLICATIONS AND PRESENTATIONS TO LEARNED SOCIETIES

MORGAN WP, HUGHES LE. The Density and Distribution of the Apocrine Glands in Hidradenitis Suppurativa. British Journal of Surgery. 66 853-856. 1979.

MORGAN WP, HARDING KG, RICHARDSON G, HUGHES LE. The Use of Silastic Foam Dressing in Advanced Hidradenitis Suppurativa. British Journal of Surgery. 67 277-280. 1980.

MORGAN WP, LEICESTER GAIL. Depilation and Deodorants in Hidradenitis Suppurativa. Archives of Dermatology 118 2 101-102. 1982.

MORGAN WP, HARDING KG, HUGHES LE. A Comparison of Skin Grafting versus Healing by Granulation following Axillary Excision of Hidradenitis Suppurativa. Annals of the Royal College of Surgeons of England. 65 (4) 235-236. 1983.

HUGHES LE, MORGAN WP. Surgery of Hidradenitis Suppurativa. Rob and Smith's Operative Surgery. General Principles, Breast and Extra Cranial Endocrines. 4th Edition. Butterworths 194-202. 1982.

The Distribution and Density of the Apocrine Glands in Hidradenitis Suppurativa. Surgical Research Society, Tripartite Meeting. Oxford. July 1979.

AIMS AND STRUCTURE OF THESIS

The work covered in this thesis is as follows:-

SECTION A

A LITERATURE SURVEY

CHAPTER I. A review of the previous literature on hidradenitis suppurativa.

CHAPTER II. A synopsis of the literature concerning the apocrine sweat glands.

SECTION B

CLINICAL STUDIES OF PATIENTS WITH HIDRADENITIS SUPPURATIVA

CHAPTER III. A record of the clinical details of the hidradenitis patients entering the study with particular emphasis on:-

3.1 The age, sex and race distribution of the patients.

3.2 The site(s) of disease at entry to the study.

3.3 The nature of any previous treatments received by the patients before entering this study, with its outcome.

CHAPTER IV. Studies to:-

4.1 Determine whether a primary association exists between iron deficiency anaemia and hidradenitis.

4.2 Determine whether an increased prevalence of diabetes mellitus or a positive family history of diabetes mellitus exists in hidradenitis patients.

4.3 Compare the distribution of the ABO and Rhesus blood groups in hidradenitis patients with those of a normal population, as evidence of a genetic mechanism in transmission of disease susceptibility.

4.4 Compare the frequency of a positive family history of hidradenitis in hidradenitis patients with a normal control population.

4.5 Compare the prevalence of acne vulgaris, sebaceous (epidermoid) cysts in hidradenitis patients, with a control population.

4.6 Compare the prevalence of hypersensitivity reactions in hidradenitis patients with a control population.

4.7 Compare the use of shaving, depilatory agents, deodorants and talcum powder, in the axillae and pubo-inguino-perineal region of hidradenitis patients, prior to the development of the disease, with that of a control population.

4.8 To examine the influence of the menstrual cycle and pregnancy upon the activity of hidradenitis.

SECTION C

STUDIES OF THE APOCRINE SWEAT GLANDS IN HIDRADENITIS

CHAPTER V. 5. To compare the surface area, diameter and numbers of the apocrine glands in the axillae of hidradenitis patients with hyperhidrosis patients and control subjects. To compare the surface area, diameter and numbers of the apocrine glands in the pubo-inguino-perineal region of hidradenitis patients with control subjects.

CHAPTER VI. 6. To develop a method of demonstrating the distribution of the apocrine glands in the axillae and pubo-inguino-perineal regions of hidradenitis subjects, pre-operatively, with the intention of facilitating their complete excision.

CHAPTER VII. 7.1 To demonstrate the distribution of the apocrine sweat glands in the axilla of hidradenitis subjects, by microscopic examination of the excised skin specimens.

7.2 To demonstrate the distribution of the apocrine sweat glands in the pubo-inguino-perineal region of hidradenitis subjects, by microscopic examination of the excised skin specimens.

CHAPTER VIII. 8. To describe the microscopic features of hidradenitis in relation to the apocrine glands.

SECTION D

SURGICAL TREATMENT

CHAPTER IX. 9.1 To assess the effectiveness of radical excision of the axillary skin, where widespread, chronic disease exists.

9.2 To assess the effectiveness of wide excision of the apocrine gland containing skin in the pubo-inguino-perineal region, in ablating hidradenitis.

CHAPTER X. 10.1 To compare healing by granulation, using Silastic Foam dressing, with split skin grafting in the healing of the axillary excisions.

10.2 To assess healing by granulation using Silastic Foam dressing, in the healing of the pubo-inguino-perineal excisions.

Each chapter is provided with a list of contents. Chapters III to X inclusive are divided into 4 sections:-

Introduction, Patients and Methods, Results and Discussion.

CONTENTS PAGE

CONTENTS PAGE

LIST OF TABLES PAGE

LIST OF FIGURES PAGE

LIST OF APPENDICES PAGE

SECTION A

CHAPTER I

HIDRADENITIS SUPPURATIVA

A REVIEW OF THE LITERATURE

CONTENTS PAGE

HISTORY

The first description of hidradenitis suppurativa is generally accredited to Velpeau, who in 1839, described superficial abscesses involving the skin of the human axillary, mammary, and perianal regions. He was unfamiliar with the association of the abscesses with the sweat glands, which had been described by Purkinje in 1833.

Verneuil, in 1854, utilising the anatomical work of Robin (1845), amplified the description of Velpeau and suggested the sweat glands as the site of the recurrent inflammation. However, it was not until 1922, when Schiefferdecker classified, named, and described the sweat glands as eccrine and apocrine, that hidradenitis suppurativa was specifically related to the apocrine glands.

The term hidradenitis originates from the Greek works Hidros-sweat, and Adenos-gland, the suffix -itis- implying an inflammatory process. Harrison in 1964, suggested that the term -apocrinitis- would be a more specific name for the condition.

1.1 INCIDENCE

Hidradenitis suppurativa is generally considered to be an uncommon condition, and the prevalence in the general population from which reported series have been drawn is unknown. However, Jackman and McQuarrie (1949), reported a series of 388 patients with hidradenitis seen over an 8 year period, lending support to the theory that the condition may be more common than is generally thought.

1.2 AGE

The maximum incidence occurs in the 2nd and 3rd decades of life, with most cases presenting for treatment in the 2nd, 3rd and 4th decades. The condition may, however, present in later decades, and Ching and Stahlgren (1965), report a significant incidence of new disease in the 4th, 5th and 6th decades. Many authors consider hidradenitis to be a condition of adult life, occurring

only after puberty, however, Tachau (1939), and Ajayi and Olurin (1970) have described the condition as occurring in boys of 4 years and 2 years respectively.

1.3 INFLUENCE OF RACE

Many authors state that hidradenitis is more common in Negroes, and O'Brien et al. (1976) makes reference to Homma (1926) in support of this claim. However, Homma studied only the relative frequency of apocrine glands in Negro and White subjects, not the relative frequency of hidradenitis. Ching and Stahlgren (1965), Jackman and McQuarrie (1949), and Tasche et al. (1975),all report a predominance of Negro subjects in their series. None of these papers, relate the prevalence of the condition in White and Negro subjects to the proportion of those races in the studied population. It may be therefore, that hidradenitis is more common in Negroes but the case for this is not proven. It is interesting that Ajayi and Olurin (1970) were able to report only 6 cases of hidradenitis seen at University College Hospital, Ibadan, Nigeria over a 12 year period. If the condition is more prevalent in Negroes, one might expect significant figures to emanate from Nigeria.

1.4 SITES INVOLVED

Hidradenitis is commonly found involving the axillae, groins, external genitalia and perianal area. However, it has been reported involving the nape of the neck, areola of the breasts, sub-mammary fold, the extremities, the peri-umbilical region, the buttocks, the temporal and peri-orbital areas of the face (Greer, 1974), and the glands of Moll (Sachs and Gordon, 1967). The terms perianal and perineal hidradenitis are used loosely by many authors, which Anderson and Dockerty (1958), point out, with reference to perianal disease, is often used to describe involvement of the scrotum, buttocks, proximomedial aspect of the thigh and the inguinal and pubic regions,as well as the specifically named site.

Bell and Ellis (1978), Knaysi et al. (1968), Ching and Stahlgren (1965), Jackman and McQuarrie (1949) and Brunsting (1939) have

reported representative series of patients with hidradenitis. The distribution of the condition at the various sites in these series is shown in Table 1. The axillae are the most commonly involved site, followed by the perianal area and the groins. Bell and Ellis (1978) and Tachau (1939) reported that 75% and 26% respectively of their patients with axillary hidradenitis had bilateral involvement of the axillae.

Most authors are of the opinion that axillary disease predominates in the female, and pubo-inguino-perianal disease in the male. Tachau (1939) and Tasche, Angelats and Jayaram (1975) reported a female : male ratio of 3 : 1, and 22 : 1, respectively in patients with axillary disease. Thornton and Abcarian (1978) and Anderson and Dockerty (1958) found a male : female ratio of 2 : 1 in 104 and 117 patients, with perianal and perineal hidradenitis respectively. Nance (1970) pointed out that women are affected with hidradenitis up to three times more commonly than men.

1.5 CLINICAL PRESENTATION

Hidradenitis Suppurativa occurs in people who enjoy generally good health. The clinical appearance of the condition can be divided broadly into 2 phases:- acute and chronic, which have been clearly described by Brunsting (1939).

1.5.1 ACUTE

The disease usually begins insidiously with pruritis, burning and local hyperhidrosis as the earliest symptoms. Later, a sensation of discomfort develops in the affected area, followed by the development of a small firm subcutaneous nodule in that area. Involution of the nodule may occur without discharging or surgical drainage; however, absorption is usually slow, and the residual skin infiltrate may be present for several weeks. After a variable time interval, new nodules appear adjacent to the original lesion. These coalesce to form a characteristic cordlike elevated band. Suppuration may not be apparent at this stage as it is invariably deep seated. A small pustule may present at the apex of the nodule, which if

TABLE 1.

THE DISTRIBUTION OF HIDRADENITIS BY SITE IN REPORTED SERIES.

	AXILLA	GROIN	GENITAL AND PERIANAL	EXTERNAL AUDITORY MEATUS	BREAST NIPPLE	SACRAL AREA	FACE	NECK
1978 Bell & Ellis 22 female 2 male	83%	42%	17%	4%	4%	-	-	-
1968 Knaysi et al. 35 female 10 male	93%	11%	18%	-	-	9%	-	-
1965 Ching & Stahlgren 10 female 19 male	69%	38%	48%	-	3%	-	3%	-
1949 Jackman & McQuarrie 197 female	72%	24%	32%	-	8%	-	-	11%
1939 Brunsting 12 female 10 male	95%	41%	86%	-	14%	-	-	-

incised drains only a few drops of thick pus. Drainage may continue for several days, before eventual cicatrization and complete healing take place.

1.5.2 CHRONIC

However, suppuration may persist and extend into the deeper layers of the subcutaneous tissues with the formation of extensive sinus tracts. Frequent remissions and relapses may occur and healing may be delayed. The disease has then entered the chronic phase. The extensive undermining and burrowing that occur throughout the subcutaneous tissue are characteristic features of the condition. Brunsting (1939) describes inversion and undermining of the cutaneous margins as occurring, leading to ulceration with destruction of the underlying subcutaneous fat and connective tissue. The ulcers are described as having rolled-in and ragged edges, with a base of healthy-appearing granulation tissue, which feels boggy to palpation. Remaining epithelial bridges connect the sinus tracts. Gangrene does not occur but fever and associated systemic disturbance in connection with recurrent bouts of regional erysipelas are not uncommon. The surrounding skin has an atrophic appearance of a deep cyanotic colour, commonly seen in chronic pyogenic infections. Eventually, extensive fibrosis of the subcutaneous tissue develops, especially in the lines of the subcutaneous tracts, giving rise to tight bands. These limit movements in the flexures, which limitation is especially prominent in the axillae.

Barron (1970) in his paper on perianal hidradenitis states that while most writers consider the spread of the pathological process to occur laterally and not deeply, this, in his experience did not hold true for the perineal, perianal, buttock, sacral and coccygeal areas. In these areas, he claimed, the process could extend deep to vital nerves and vessels, and into the anterior sacral and coccygeal spaces. Fistulae to deeper tissues, such as the peritoneum, anus, rectum, bladder, testis and urethra, having been described by Moschella (1966). Ward et al. (1974), in their report of 2 patients with severe perineal hidradenitis found that

the disease did not extend deep to the perineal membrane. Brunsting (1939) described a case with perianal disease as having a fistula in ano. Jackman (1942) considered that when the anorectum was involved, the fistula usually penetrated the anus distal to the dentate line. Anderson and Dockerty (1958) concluded that anal fistula secondary to hidradenitis was rare in their series of 117 patients with perianal hidradenitis. Culp (1983) described hidradenitis as involving the distal two thirds of the anatomic anal canal, because the proximal portion was devoid of hair follicles and accessory glands. An anal fistula lacking continuity with the cryptoglandular units of the dentate margin or intersphincteric space or both being suggestive of hidradenitis. The fistula of hidradenitis is a track that originates in a pitlike scar, usually epithelialised, within the skin of the distal anal canal, and progresses beyond the anal verge superficial to the internal sphincter muscle.

Hidradenitis commences usually at one site, but often progresses in the areas previously mentioned, to involve multiple other sites over a period of time. After years of activity, the condition often becomes quiescent, possibly because of destruction of most of the apocrine glands of the body.

In the meantime, the chronic course of the disease with pain, constant foul-smelling discharge and disfigurement leads to considerable physical discomfort, economic loss, social embarrassment, mental distress and marital disharmony.

1.6 AETIOLOGY AND PATHOGENESIS

The essential cause of hidradenitis suppurativa is still uncertain. The proposed mechanisms of the condition proffered in the literature appear to fall into 3 categories: (a) the most widely accepted mechanism is keratinous plugging of the follicular orifice and its tributary, the apocrine gland duct, with obstruction and dilatation of the apocrine tubules and superimposed bacterial infection; (b) that the condition results from bacterial infection of hair follicles obstructed by hyperkeratinisation, and that the

condition can arise in areas of skin lacking apocrine glands, apocrine gland involvement in hidradenitis being purely incidental; (c) that the apocrine glands are not primarily involved in hidradenitis but become secondarily involved by extension of infection from the surrounding subcutaneous tissue.

(a) The localisation of hidradenitis in its most classical form to areas of the body (e.g. the axillae and groins) that have the distinction of possessing concentrations of apocrine sweat glands led to the initial connection between the apocrine glands and hidradenitis. Many workers have found histological interpretation of skin sections removed from areas of florid hidradenitis unhelpful. Since the microscopic field usually shows dense infiltration of the subcutis with chronic inflammatory cells, and the absence of apocrine glands in the specimen could be a result of no apocrine glands being originally present, or that being originally present, they have been destroyed by the disease process.

Brunsting (1939) studied sections of excised hidradenitis skin and considered that the initial inflammation was confined to the apocrine glands, which were distended with leukocytes. He considered the infection to proceed through the subcutis by means of the lymph channels; distended lymph spaces containing many leukocytes and cocci being visualised. There was little peri-glandular inflammation in some areas but in other areas, the peri-glandular tissue showed considerable cellular reaction without involvement of the wall of the gland. If these latter areas were followed in serial section, he considered that invasion of the wall of the gland from without could be easily demonstrated. As the disease progressed through the subcutis the eccrine glands became similarly involved. While the blood vessels presented no changes early in the course of the condition, in the later stages a peri-vascular infiltrate of plasma cells and lymphocytes, with oedema of the walls of the vessels could be seen. Likewise in the later stages, large pale-staining irregularly-shaped giant cells with a deep-staining eccentrically-placed nuclei could be seen in the centre of the disease process. Foreign body giant cells were also present. Brunsting found that the upper parts of the subcutis and epidermis were not involved

until extensive destruction had occurred throughout the subcutis.

Gordon (1978) described hidradenitis as a poral occlusion disease with subsequent bacterial infection, the infection arising in the pilo-sebaceous follicle and secondarily invading the contiguous apocrine glands. Following apocrine ductal occlusion, microscopically, one sees dilatation of the apocrine gland, and acute inflammatory cell infiltrate. The dilatation eventually results in rupture of the apocrine gland with spread of the infection to adjacent glands.

Hurley and Shelley (1954) demonstrated experimentally that simple occlusion of the apocrine glands did not result in hidradenitis, despite the production of sweat retention cysts. They also found that rupture of these cysts with the escape of sterile sweat into the dermis produced an epithelioid histologic response but no inflammatory changes. They concluded that bacterial infection within the apocrine gland, in addition to poral closure, was a requisite for the appearance of hidradenitis.

Shelley and Cahn (1955) attempted to overcome the difficult interpretation of the pathogenesis of hidradenitis by reproducing the disease experimentally. The axillae of 12 normal male adult subjects, aged 20 - 40 years, were used as the test sites. A perforated belladonna adhesive tape was applied to one axilla, which had been manually epilated. The other axilla served as the control site. One week later, they took biopsies from both axillae, which were serially sectioned and stained with haematoxylin and eosin. In every subject, apocrine anhidrosis developed in the taped areas, which was confirmed by local injections of adrenalin. Three of the 12 subjects developed clinical hidradenitis, with small deep tender nodules sharply localised to the tape site. Their microscopic examination of the biopsy specimens showed keratinous plugging of the apocrine sweat duct, duct dilatation and severe inflammatory changes clearly limited to a single apocrine gland unit. The adjacent apocrine, eccrine and sebaceous glands were normal, as were the hair follicles. Shelley and Cahn considered that the adhesive tape led to maceration, producing a keratotic plug in

the apocrine duct orifice. The normal bacterial surface flora became trapped beneath this plug and finding apocrine sweat an excellent milieu, thrive. Numerous polymorphonuclear leukocytes enter the duct and gland producing a local purulent reaction. While Shelley and Cahn's experiment ended at this point, it is not difficult to conceive its progression to the situation seen clinically, with spread through the dermis. The experiment also suggested that a predisposition to hidradenitis is, also, probably necessary, as only 3 of the 12 subjects to whom the tape was applied developed clinical hidradenitis.

This mechanism of poral closure, followed by bacterial infection of the apocrine glands, in the pathogenesis of hidradenitis, is supported clinically by the report of Spiller and Knox (1958) of the secondary development of hidradenitis in Fox-Fordyce disease, where the apocrine ducts become occluded by mucinous material and also, by that of Stone (1976), who described hidradenitis developing in acanthosis nigricans, where hyperkeratosis may lead to poral closure. Steiner and Grayson (1955) suggested that in cases of familial hidradenitis, inherited malformation of the ducts may be involved.

Brunsting (1952) drew attention to the frequency with which hidradenitis, acne conglobata and dissecting cellulitis of the scalp occur in the same person. All 3 disease processes share hyperkeratotic occlusion of the follicular orifice, functional glandular hyperplasia of the apocrine gland and pilosebaceous apparatus, double comedo formation, and bacterial invasion leading to suppuration and undermining of the loose areolar tissue, with eventual healing resulting in cicatrization and occasional keloid formation.

(b) Anderson and Dockerty (1958) felt that the concept that hidradenitis was in some way related to the apocrine glands, stemmed from the fact that the disease was found most often in regions where apocrine glands were said to be. With a view to investigating this concept, they studied 261 microscopic sections taken from 64 patients undergoing excision of perianal hidradenitis. Eccrine sweat glands were visualised in 59 of the 64 cases, but typical

apocrine glands were seen in only 7 cases. Anderson and Dockerty felt that the infrequency with which the apocrine glands were seen, could not be explained by the complete destruction of the apocrine glands by the inflammatory process, as some of the sections were taken from the least involved zone in each case. Periglandular inflammation was seen frequently about the apocrine, eccrine, sebaceous glands and the hair follicles, but it was thought that this mainly represented peri-vascular exudate involving the small vessels about the coils of the glands. In no section was evidence of inflammation found within the coil of a sweat gland, either apocrine or eccrine in the absence of periglandular inflammation. On the contrary, inflammatory exudate could be noted about the sweat glands, while the lumens and lining cells of those glands were uninvolved. Anderson and Dockerty concluded that the apocrine glands were not of great importance in the pathogenesis of hidradenitis, and that their involvement was purely coincidental.

Weiner et al. (1976) described a case of hidradenitis occurring on the lower leg, an area that is generally thought not to contain apocrine glands. They suggested that the main factor in the pathogenesis of the disease was follicular occlusion, with superimposed infection, and that if apocrine glands were present in the affected area, their involvement was secondary. However, the presence of apocrine glands was not necessary for the development of the condition.

(c) Brunsting (1939) reported that in two of his 22 cases, hidradenitis developed secondary to infection of the fingers or hand, the resulting axillary lymphadenitis and suppuration spreading to involve the apocrine glands secondarily. Other authors have reported a minority of similar cases, (Nance 1970, Paletta 1963, Harrison 1964). Tachau (1939) found the association between hidradenitis and hand infections with lymphadenitis to be exceptional. In his series of 107 cases, the association was seen only twice but in both these cases, the axillary abscesses were present in the axilla contralateral to the hand infection.

A review of the literature shows that most authors consider the

mechanism of hidradenitis to be (a), that is, keratinous plugging of the apocrine duct, with superimposed bacterial infection of the apocrine gland, and that the apocrine glands are primarily involved in the pathogenesis of hidradenitis.

For this reason, a summary of the anatomy, distribution and physiology of the apocrine glands is given in Chapter II.

1.7 AETIOLOGICAL FACTORS

Many factors, both local and systemic, have been suggested to contribute to the production of hidradenitis.

1.7.1 LOCAL FACTORS

Poor hygiene, has been advanced by many authors as a contributing factor. Mustafa et al. (1980) state that most patients with hidradenitis are overweight, and that the obesity may predispose to hidradenitis because of increased friction, warmth and moisture making it more difficult to maintain personal hygiene.

Both mechanical and chemical trauma are frequently advanced as predisposing causes. The plucking or shaving of the axillary hair, may remove the stylet which helps the drainage of the apocrine glands. The application of chemical depilatory agents, deodorants and anti-perspirants may lead to chemical inflammation, resulting in poral stenosis.

Steiner and Grayson (1955) found that 50% of their acute cases of hidradenitis gave a history of mechanical or chemical trauma. These included shaving, a plaster cast for a fractured humerus, friction from a limb prosthesis, and chemical irritation.

Christensen (1950) described a case of perianal hidradenitis, which arose, after the skin in that area was contaminated by discharge from a pilo-nidal cyst. It was suggested that contamination from an adjacent infected source could play a part in the initiation of hidradenitis.

1.7.2 IMMUNE DEFENCE MECHANISMS

In the presence of chronic, recurrent infection, a deficiency in either humoral or cellular defence mechanisms would be an obvious possibility. Dvorak et al. (1977) studied granulocyte phagocytic function, intracellular killing capability, chemotaxis, and granulocyte adherence in 7 patients with active hidradenitis. They were unable to demonstrate any abnormality in any granulocyte or cell-mediated immune function. All 7 patients were found to have normal immunoglobulin levels and elevated total haemolytic complement. They concluded that hidradenitis was a localised chronic infection of the apocrine glands, without a generalised defect in host defence. However, Ginder et al. (1982) report one patient with hidradenitis who had a defect in polymorphonuclear leukocyte killing of bacteria associated with low levels of intracellular cyclic GMP. This defect was corrected with a cholinergic agent in vitro. Treatment of the patient with the cholinergic agonist, bethanechol chloride, resulted in prolonged clinical improvement, normal bactericidal function, and normal levels of intracellular cyclic GMP.

McDaniel and Welton (1984) described a notable improvement in 2 patients with hidradenitis, treated with Tolmetin sodium, a pyrrole acetic acid derivative and a non steroidal inflammatory agent. Immunological testing suggested that some of these patients exhibited increased suppressor T cell activity, which returned to normal during treatment.

Bell and Ellis (1978) found an abnormally high incidence of atopic reactions in their series of patients. They found that 25% suffered from hay fever, compared with the expected incidence of less than 10% in the general population; 12.5% had an allergy to penicillin, and a further 29.2% had a history of allergy to Elastoplast; the major allergen in Elastoplast adhesive being colophony. Bell and Ellis in a personal communication with Smith and Nephew Ltd., ascertained the expected incidence of allergy to colophony to be around 2%. These findings suggest an association between atopy and hidradenitis.

1.7.3 ENDOCRINE FACTORS

The apocrine glands, generally become active after puberty, reach their peak during the reproductive years, and decline slowly during the climacteric. This coincides with the appearance of hidradenitis after puberty, its maximum incidence during the reproductive years and the decline of the disease during the climacteric.

Brunsting (1952) describes an excess of androgen as stimulating the surface epithelium and the sebaceous glands, producing a seborrheic state with hyperkeratinisation and impaction of the hair follicles, oestrogen having the opposite effect of inhibiting keratinisation and the activity of the sebaceous glands.

Eunuchs and eunuchoids do not develop acne, and Brunsting (1952) quotes Sulzberger (1941), who reported that one of his patients who received androgen therapy for eunuchoidism, developed a flare up of axillary hidradenitis with each treatment. Sulzberger also reported a coincidental androgenic stimulation of the sebaceous glands with the appearance of acne. Curtis (1948) attributed the presence of hidradenitis in a 48 year old woman, with pituitary basophilism, to increased androgenic stimulation.

In contrast, Cornbleet (1952a) reported improvement or cure in 2 women with Fox-Fordyce disease and 8 with hidradenitis, in an uncontrolled trial of testosterone propionate therapy. The report is unconvincing, and any improvement could be explained by remissions that occur without treatment, as part of the natural course of the disease.

The fluctuating level of the sex hormones during the menstrual cycle and pregnancy are of interest to those studying an endocrine influence in hidradenitis. Anderson and Dockerty (1958) reported that 5 of their 41 female patients with perianal hidradenitis developed exacerbations pre-menstrually. Hurley and Shelley (1960), and Harrison (1964) report exacerbations of hidradenitis in women a day or two before their menstrual period. It has been suggested that this is due to increased apocrine gland activity during the menses.

Cornbleet (1952b) reported the cases of one woman with Fox-Fordyce disease and of 2 with hidradenitis who had remissions or were greatly improved during their periods of pregnancy. The disease relapsed in 2 patients following delivery, and the third patient was lost to follow up. Cornbleet suggested that the amelioration of apocrine gland diseases during pregnancy was due to the apocrine glands being found more often in the quiescent phase during the gravid state.

Despite these observations, no altered hormone levels have been consistently described in hidradenitis and none of the available hormone products known to be increased during pregnancy have been of any value when administered to patients with hidradenitis, (Cornbleet (1952b). Hurley and Shelley (1960) failed to produce hidradenitis by local or systemic administration of androgens or oestrogens, or by the implantation of androgen or oestrogen pellets.

It would seem that the relative balance of various hormones may be more important in influencing the activity of hidradenitis, than the absolute level of any particular hormone.

1.8 ASSOCIATED CONDITIONS

Brunsting (1952) described the association between chronic hidradenitis, dissecting cellulitis of the scalp, and acne conglobata involving the face, neck and back, the basic lesion in all 3 conditions being follicular occlusion caused by hyperkeratotic plugging.

The most commonly reported associated lesion in hidradenitis is acne vulgaris. Steiner and Grayson (1955) reported that 9 of 12 patients with chronic generalised hidradenitis showed either active lesions or scars of acne. Conway, Stark and Climo (1952) reported that 70% of patients with hidradenitis had active acne or evidence of severe past acne. However, Anderson and Dockerty (1958) found acne present in only 30% of their perianal hidradenitis patients.

It is not clear from the literature, as to whether there is an

association between hidradenitis and pilonidal sinus or cysts. Anderson and Dockerty (1958) reported that a diagnosis of pilonidal disease had been made in 16 of their 117 patients with perianal disease. Fourteen of these 16 patients gave a history of having received surgery for pilonidal disease at another centre. Anderson and Dockerty made the diagnosis of pilonidal disease, themselves, in two instances only. They later changed the diagnosis to hidradenitis of the post sacral region in one of these cases. Steiner and Grayson (1955) considered 2 of 12 patients with chronic generalised hidradenitis to have pilonidal abscesses. Knaysi et al. (1968) found what they considered to be an increased incidence (9%) of sebaceous cysts in their hidradenitis patients. However, none of these studies compare the incidence of pilonidal sinuses or sebaceous cysts in hidradenitis, with that in an age and sexed matched control population, and are, therefore, little help in determining whether an association exists between hidradenitis and these conditions.

According to Mustafa (1980) diabetes mellitus has not been shown to predispose directly to hidradenitis. However, diabetes was detected in 10% of Chapman's (1972) series of patients, and was noted in the relatives of 3 of Bell and Ellis' (1978) patients (12.5%). Mackenna and Lehmann (1960) examined the glucose tolerance curves in 7 patients with hidradenitis, with an inability to utilise glucose normally. Five cases showed a flat blood sugar curve; 1 patient showed a lag curve and another a diabetic curve. The patients with flat curves and the one patient with a lag curve showed clinical improvement when given oral riboflavine. Riboflavine was not administered to the patient with a diabetic curve. None of these studies clarifies as to whether an association exists between diabetes mellitus and hidradenitis.

Bergeron and Stone (1967) described 4 cases of interstitial keratitis as occurring in a series of 62 patients with hidradenitis. Interstitial keratitis is generally considered to be a delayed allergic corneal reaction to congenital syphilis, usually presenting at 5 - 12 years of age. However, granulomatous disease e.g. tuberculosis, leishmaniasis, lepromatous leprosy and sarcoidosis are also causative factors. In Bergeron and Stone's cases hidradenitis

had preceded the keratitis by 5, 7, 8, and 9 years respectively. All 4 patients had, in addition to severe hidradenitis at multiple sites, a microcytic hypochromic anaemia and increased gamma globulin levels. Three of 4 patients were serologically negative for syphilis. Syphilis was present in the fourth, and was of the acquired type. None of the patients showed the stigmata of congenital syphilis.

A miscellany of other associated conditions have been reported by various authors. Adams and Haisten (1972) stated, without producing supporting evidence, that a high serum cholesterol was usual in hidradenitis. Marks (1945) reported that hidradenitis patients were asthenic and underweight and failed to gain weight readily. They complained of excessive fatigue, had subnormal morning temperatures and their skin was sallow and oily. Their basal metabolic rates were low and laboratory data showed hypothyroidism. Their diet was rich in lipids, and a constant feature was hypercholesterolaemia. Their condition improved when treated with an adequate calorie diet, low in lipids accompanied by thyroxine supplements. Mustafa (1980) stated that some patients with hidradenitis were found to have a high metabolic rate. Mustafa (1980) considered obesity to be a significant association in hidradenitis patients, as did Steiner and Grayson (1955). However, nowhere in the literature are there any figures to confirm or refute this. Chalfant and Nance (1970) in reporting a case of a 30 year old coloured male with hidradenitis involving the inguinal and perianal areas, state that the condition is often associated with abnormalities of steroid metabolism such as Cushing's disease and virilism. However, again, no supporting data or references to any other work are given in support of this statement.

1.9 FAMILY HISTORY

Little attention has been paid in the literature to the family history of hidradenitis patients, and as to whether if such a family history exists, it is as a result of a common environment or is genetically based. Knaysi et al. (1968) reported a family history of hidradenitis in 3 of 18 patients specifically questioned. Weiner et al.'s (1976) patient with the diagnosis of hidradenitis occurring on the leg in addition to disease at the more classical sites,

had a strong family history of perianal abscesses.

1.10 COMPLICATIONS

1.10.1 ANAEMIA

Tennant et al. (1968) reported that in a study of 42 hidradenitis patients, 10 patients without concomitant systemic disease were found to have a marked anaemia. The haemoglobins were 10 gms./100 mls. or less, and the anaemias of an iron deficiency pattern. All 10 patients had suffered from hidradenitis involving the buttocks and groins for a minimum period of 2 years. Improvement of the anaemia occurred with surgical treatment, but not with iron therapy. Gordon (1978) considered that the failure to respond to iron therapy was due presumably to decreased serum transferrin levels, that the severity of the anaemia increased in proportion to the number of organisms in the infected area, and that the anaemia tended to be present only in the more severe cases of perianal hidradenitis. Twenty of the 40 patients studied by Tennant et al. had serum protein electrophoresis; 16 of the 20 patients showed elevated y-globulin fractions, and 13 of the 16 showed reversal of the albumin-globulin ratio. Moschella (1966) considered the anaemia in hidradenitis to be identical to that caused by other chronic diseases or malignant processes.

1.10.2 MALIGNANCY

As with any chronic, irritating process, malignant change may develop in areas involved with hidradenitis. The first account of squamous-cell carcinoma arising in hidradenitis was by Anderson and Dockerty, who in 1958, described 2 cases of squamous-cell carcinoma arising in patients with hidradenitis of 25 and 32 years, duration. Jackman (1942) in his series of 125 cases of perianal hidradenitis, found 4 who developed squamous-cell carcinoma, an incidence of 3.2%. The cases were all of long duration, varying between 19 to 32 years. Donsky and Mendelson (1964) likewise described squamous-cell carcinoma arising in long-standing perianal hidradenitis. Gordon (1978) described squamous carcinoma arising in the post-sacral skin of

a 28 year old black female, after 17 years of chronic hidradenitis. Further reports of squamous carcinoma developing in long-standing perianal hidradenitis have come from Thornton and Abcarian (1978) and Alexander (1979). Alexander reported a case of squamous carcinoma arising in the thigh and perineal area of a 40 year old white male who had suffered from hidradenitis of the axillary, inguinal and perineal regions for over 20 years. Biopsies taken from this case suggested the origin of the tumour to be multifocal. Despite wide excision of the tumour-containing area, this patient developed widespread metastases and died.

The reported cases of squamous carcinoma developing in hidradenitis have all occurred in cases of pubo-inguino-perianal disease of long duration; the shortest period of time between the development of hidradenitis and carcinoma being 8 years. Three of Jackman's (1942) 4 cases were stage one, and were cured by wide local excision. The 4th case was stage two, and died with widespread secondaries. Alexander (1979) recommended wide excision of chronically-involved areas of hidradenitis to prevent the development of malignant change.

1.10.3 GENERAL COMPLICATIONS

The seriousness of perianal hidradenitis, as compared to axillary hidradenitis, can be appreciated from the frequency in the former of severe anaemia, fistulation to underlying organs and the development of squamous carcinomas. Moschella (1966) reported the death of a patient, secondary to severe anaemia, hypoproteinaemia and amyloidosis with extensive fistula formation to the pelvic organs.

1.11 MICROSCOPY OF HIDRADENITIS

Woods et al. (1972) made a histological study of specimens of skin obtained from operation specimens of excised hidradenitis from the labia majora, mons pubis and groins. They found the apocrine glands to be contained in areas of acute and chronic inflammation; while in other areas the apocrine glands were uninvolved. Many glands were dilated and contained inspissated material, while their lumens contained an abundance of polymorphonuclear leukocytes.

Micro-abscesses were scattered throughout the specimens, exhibiting total destruction of the glandular tissues in these areas, with surrounding plasma cells and lymphocytes.

Anderson and Dockerty (1958) in studying histological sections of skin taken from patients with perianal hidradenitis, found an inflammatory cell infiltrate consisting of plasma cells, with some lymphocytes and fixed connective tissue cells in nearly all the cases studied. The distribution of cellular infiltrate was similar in most cases. Perivascular infiltration was noted in 42 of the 64 surgical specimens. Zones of diffuse cellular infiltration were present in 39 of the patients, and giant cells were noted in these zones in 12 instances. Cellular infiltrate was noted frequently just beneath the epidermis, and in the tissue and lymphatic spaces. Periglandular inflammation was frequently observed about the apocrine glands, but also about the hair follicles, and eccrine and sebaceous glands. Anderson and Dockerty considered that much of the periglandular infiltrate consisted of perivascular infiltrate of the small blood vessels surrounding the glands. While glandular lumen free of cellular content in the presence of periglandular infiltrate could be observed, in no section was involvement of the glandular lumen seen in the absence of periglandular infiltration. They concluded that the sweat glands are involved from without in hidradenitis, and that involvement of the apocrine glands in hidradenitis is purely coincidental.

Harrison (1964) examining axillary specimens of hidradenitis histologically, described the presence of cystically dilated apocrine glands with diffuse chronic inflammation.

Brunsting (1939) described the occurrence in the inflammatory cell infiltrate of large pale-staining irregularly-shaped giant cells, with deeply-staining eccentrically-placed nuclei. He, also, noted that foreign body giant cells may be present.

1.12 BACTERIOLOGY OF HIDRADENITIS

According to Gordon (1978) bacteriological cultures of material obtained from cases of hidradenitis nearly always demonstrate mixed

organisms, with coliforms predominating in the perianal areas and staphylococci predominating in other areas. Duncan (1976) considered that the bacteriological finds varied with the stage of disease being studied, Staphylococcus aureus being the predominant organism in acute cases. In chronic cases, the variety of organisms was greater and usually consisted of enteric organisms. The use of antibiotics, also, causes a selection of resistant organisms, with further variation in the bacterial flora of the area. Anderson and Perry (1975) considered that Staphylococcus aureus and Streptococcus viridans were the main organisms involved in the pre-antibiotic era. Harrison (1964), Piggott and Ellis (1975) and Tachau (1939) all considered Staph. aureus to be the predominant organism.

Goldsmith (1950) failed after repeated attempts to culture the tubercle bacillus from hidradenitis specimens, as did Greely (1950).

Smith and Ropes (1945) reported repeated culture of the anaerobe bacteroides from a patient with hidradenitis. Beigelman and Rantz (1949) similarly reported obtaining a heavy growth of bacteroides from the draining sinuses of an 18 year old woman with axillary hidradenitis. Interest in the role of anaerobic infection in hidradenitis then appeared to wane, until very recently. Leach et al. (1979) reported a series of 52 patients suffering from axillary abscesses, amongst which there were 7 cases with clinical hidradenitis. A variety of anaerobes were isolated from 5 of these cases and skin flora alone in 2 cases. The anaerobes consisted of Peptococcus, Bacteroides melaninogenicus, Bacteroides corrodens, and Bacteroides fragilis. Brenner and Lookingbill (1980) described 5 cases of chronic perineal hidradenitis, in which, when anaerobic cultures were performed, moderate to heavy growths of bacteroides were found. These growths, consisted almost exclusively of Bacteroides melaninogenicus, Bacteroides fragilis or both. However, Highet et al. (1980) felt that while anaerobes were involved in hidradenitis; the Gram-positive aerobic bacteria, also, had a significant role to play. They isolated bacteroides species in 5 of 14 patients with active perineal hidradenitis, but were more impressed with the possible role of Strept. milleri (Lancefield group F), which they isolated in 8 of 14 patients. Staph. aureus was considered

to be a significant treatable pathogen in 7 of these 14 patients. Other organisms isolated included Proteus species, anaerobic streptococci, a group B streptococcus and a faecal streptococcus.

A review of the literature suggests that nearly all authors would consider that the bacteria play a secondary role in hidradenitis; the primary event being occlusion of the apocrine duct and follicular orifice.

1.13 DIFFERENTIAL DIAGNOSIS

The differential diagnosis of hidradenitis suppurativa varies, depending on where the lesions are, and upon whether the disease is in an acute or chronic phase. In general, when the axillae are involved the diagnosis of hidradenitis is easier, but when the perianal area is involved, the diagnosis can be difficult.

Acute lesions must be distinguished from:- furuncles, carbuncles, dermoid cysts, pilonidal sinus, lymphadenitis, sebaceous cysts, acne, perianal abscess, ischio-rectal abscess, cutaneous blastomycosis, cellulitis and erysipelas.

Chronic lesions need to be distinguished from:- tuberculosis, lymphogranuloma venereum, granuloma inguinale, perianal fistulae, nocardia, actinomycosis, tularaemia, cat scratch disease, and noduloulcerative syphilis.

All sinus and fistula-forming conditions in the perianal area may be confused with hidradenitis, including Crohn's disease. Christensen (1950) reported 8 cases of hidradenitis originally believed to be anal fistulae. What were considered to be perineal urethral fistulae (Carter, 1962) or recurrent pilonidal cysts (Jackman and McQuarrie, 1949) may finally prove to be hidradenitis in disguise.

The diagnosis rests upon obtaining a detailed history from the patient, with careful examination of the lesions. Conditions mentioned above that can be confused with hidradenitis should be excluded by the appropriate investigations where available. Perianal

disease may require examination under anaesthesia with biopsy of the lesions and probing of the tracks for a confident diagnosis to be made. Rectal mucosal biopsies and radiological investigation of the rectum, colon, and small bowel may be necessary where inflammatory bowel disease is suspected. Cystograms and urethrograms may be required to ascertain whether, fistulae to the bladder or urethra truly exist.

1.14 TREATMENT OF HIDRADENITIS SUPPURATIVA

The ideal treatment for hidradenitis has yet to be found, a proposition which is supported by the multitude of treatments suggested by various authors.

Early, acute disease is often regarded as a minor skin infection and the patient is treated accordingly. Classically the patient will respond initially to antibiotics, wet warm compresses, local cleansing with hexachlorophene or povidone iodine, and incision and drainage of individual abscesses. Eventually a large proportion of the patients will move into the chronic phase with regular flare-ups and extension of the disease. Mustafa (1980) considered antibiotics to be of use in the acute stage, when continued for an adequate duration and based upon culture and sensitivity studies. However, a review of the literature suggests that only one controlled trial of the use of antibiotics in the treatment of hidradenitis has ever been performed, Clemmensen (1983), who showed a symptomatic improvement with the application of topical clindamycin.

Many authors counsel their patients to be scrupulous about personal hygiene and to avoid the use of shaving, tight clothing, chemical depilatories, deodorants and anti-perspirants. Diets, sulphur baths, infra-red therapy, ultra-violet light (Bell and Ellis 1978); neoarsphenamine and injection of whole milk (Brunsting 1939) have all been advocated for the treatment of hidradenitis at some time. Oestrogens may be prescribed to women with menstrual abnormalities and some prescribe them to males until side effects appear (Mustafa 1980). Cornbleet (1952a) produced an unconvincing report of the improvement of hidradenitis in 8 women following the administration

of testosterone propionate. Danto (1958) in an uncontrolled trial used systemic hydrocortisone in doses of 40 - 80 mg. daily over short periods, in the treatment of 4 patients with axillary hidradenitis, with good results. No recurrence of disease had occurred at one year. Even insulin and thyroxine have been tried but with no success (Wynn-Williams 1953).

Brunsting (1939) suggested that Typhoid vaccine may be considered in the treatment of hidradenitis. Arnold (1955) described the use of Piromen, a bacterial polysaccharide derived from Pseudomonas, in the management of 16 patients with early axillary hidradenitis of 2 - 30 days duration (mean 9). Ten patients were cured or improved by the treatment. The series was uncontrolled and no follow up appears to have been undertaken. In a recent report, Kress et al. (1981) treated 8 patients, 7 with hidradenitis and one with recurrent staphylococcal abscesses, who had all previously failed to respond to antibiotics, with staphylococcal lysate. Seven of the 8 patients reported an improvement in their condition. Side effects were reported to be minimal and included rash, vertigo, malaise, chills, nausea, fever and headache. The authors concluded that staphylococcal lysate was a useful adjunct in the treatment of hidradenitis. Mustafa (1980) considered that toxoids and vaccines were of little value, because many different organisms were usually implicated and the variety changed with time.

Jones, Cunliffe and King (1982) treated 3 hidradenitis patients with 13-cis-retinoic acid, following good responses in patients with cystic acne. There was no improvement in the severity of their disease.

Gordon (1978), in a review of hidradenitis, considered that the results obtained by X-ray therapy in the treatment of early hidradenitis were useful. Schenck (1950) administered treatments of on average 100 - 200 roentgens in a cone of 10 by 10 cm. at a target distance of 50 cm. in cases of axillary hidradenitis. In hyperacute cases, 100 roentgens and in chronic cases 150 - 200 roentgens were given at one sitting. Each axilla was irradiated 3 times weekly for 5 - 10 treatments, to a total dose of 1,000 - 1,200 roentgens. A temporary epilatory effect usually occurred but

hair regrowth was present in 2 - 3 months. Schenck followed 54 treated cases for at least 3 months after the last X-ray treatment with no recurrence. While these results may be regarded as encouraging, it should be noted that in addition to the very short follow up undertaken in this study, that the patients treated had early hidradenitis. The duration of the disease, at presentation for treatment, varied from 2 weeks to 11 months, with an average duration of 1.4 months. Zeligman (1965) used a single dose of 450 - 500 roentgens resulting in temporary epilation. Fives cases with axillary hidradenitis were treated; the duration of disease in these cases varying from 6 months to 3 years. No recurrence had occurred in these cases at a follow up varying from 9 months to 6 years (median follow up 4 years). Tachau (1939) considered X-ray therapy to be the treatment of choice in chronic cases of axillary hidradenitis. One hundred to 120 roentgens were sufficient to give relief of pain within 2 - 3 days and for the arm to be moved without restriction. More resistant lesions required that dose to be repeated once or twice at intervals of 10 days. Tachau claimed that complete cure was almost invariably provided by this procedure, even in cases of long duration which had undergone extensive surgical procedures without success. From 1931 - 1939, Tachau treated 37 patients with this regime. Twenty-one per cent were cured after 100 - 120 roentgens, 27% after 200 - 240 roentgens and 46% after 300 - 360 roentgens. In 2 patients residual disease required further X-ray treatment after an interval of 6 or more weeks. No recurrence occurred in this group; however, recurrences had occurred in 3 of 57 patients treated before 1931, and this was attributed to less stringent control of the dose of X-ray therapy. However a number of authors including Conway et al. (1952) and Wynn-Williams (1953) have commented on patients with hidradenitis, recurrent after X-ray therapy, presenting to them for surgical management.

All authors are of the opinion that once the chronic stage of the disease is reached, the medical measures described above are of little benefit, (Anderson and Dockerty 1958; Steiner and Grayson 1955; Shaughnessy et al. 1972), and that surgical management is necessary. Antibiotics have only a minor role to play in the

management of chronic hidradenitis. Mustafa (1980) recommends that the appropriate antibiotic should be commenced prior to excision of the disease and continued post-operatively, and as stated previously by Anderson and Perry (1975) it is neither necessary nor possible to postpone surgery until the infection is cleared. Brenner and Lookingbill (1980) suggested that when bacteroides are isolated from perineal hidradenitis, antibiotics active against bacteroides e.g. Clindamycin, Metronidazole, might reduce the foul-smelling discharge and improve the chances of successful surgery.

Incision and drainage may be used for localised lesions when acutely tender; however, as pointed out by Shaughnessy (1972), in the face of recurrent disease the surgeon should move to early definitive excisional treatment and spare the patient many multiple drainage procedures which will not result in cure. Some authors e.g. Greely (1951) suggest that where chronic localised lesions exist, they may be locally excised and if the resulting small defect is clean, it may be closed primarily under antibiotic cover using a technique such as Z-plasty. There are no detailed reports of the results of local excision in chronic disease with adequate follow up in the literature and it is difficult to assess the effectiveness of this technique. However, the general impression gained from the literature is that the chance of recurrence is high after local excisions. Mullins et al. (1959) described a technique of deroofing all sinuses in axillary and perineal hidradenitis, achieving adequate drainage, followed by currettage of the sinus lining and electrocoagulation of the exteriorised area with bipolar current. This procedure was carried out in 35 patients, with improvement but not necessarily cure in all. The time to complete healing varied between 3 weeks and 3 months, with an average of 4 - 6 weeks. However, the success of this procedure is difficult to assess, as no details of long-term follow up were given, except that it appeared that some of the patients would later require wide excision.

Most surgeons would now agree with Shaughnessy (1972) that all modes of therapy short of total excision of the apocrine gland-containing skin in the diseased area are temporizing. In the case of the axilla, this is generally regarded as being the hair bearing

area. The definition of the apocrine gland-containing skin in the pubo-inguino-perineal area is more difficult.

In the case of the axilla Anderson and Perry (1975) considered total excision of the axillary hair bearing area as essential to prevent the development of recurrence. They excised an ellipse of all the axillary hair-bearing skin at 90° to the long axis of the arm. All indurated tissue was excised often down to the axillary fascia. The rationale behind removing all the axillary hair-bearing skin is that the apocrine glands empty into or adjacent to the hair follicles, and as long as a single apocrine gland is left, there is a chance of recurrence. In areas, other than the axilla e.g. groins and perineum, wide excision of all diseased tissues with a margin of normal tissue are recommended by most authors. The excisions should include all abscess cavities and sinus tracts down as far as the deep fascia. It is rarely necessary to proceed deep to the fascia, as the disease process is nearly always superficial to this layer. Ariyan and Krizek (1976) performed generous excisions of chronic inguinal and perineal hidradenitis placing elliptical incisions, directed along the skin folds. Anderson and Dockerty (1958) considered that a sympathetic relationship may exist between the various sites involved by hidradenitis, and that one may be able to prevent the appearance of hidradenitis at another site or produce a remission of mild disease at that site, by surgical excision of severe hidradenitis at the primary site. Greely (1951) suggested that where hidradenitis involved many different sites in the same patient, that it was wiser to remove individual areas at separate operations, to minimise the risk of bacterial embolisation. Donsky and Mendelson (1964) and Alexander (1979) considered wide surgical excision of the diseased area to be indicated, not only for eradication of the disease process but to prevent malignant change occurring in that area.

Following excision of the axillary skin, the resulting defects have been closed primarily, by the interposition of various skin flaps, by split skin grafting and by healing by granulation. Greely (1951) in a paper on the plastic surgical treatment of hidradenitis advocated the immediate grafting of large, but grossly clean axillary

defects, with the application of split skin grafts being delayed to the 10 - 14th post-operative day in the case of extensive and contaiminated wounds. However, there are no details of the number of patients treated in this manner or of the outcome of the treatment in this paper. Hartwell (1975) advocated the use of a stapling gun for the fixation of split skin grafts to the margins of the skin defect. Knaysi, Cosman and Crikelair (1968) performed 70 operations in the axillary region in 35 patients. In those patients with a small area of involvement, a local excision with primary closure was performed; for generalised but superficial disease, the entire hair-bearing area was excised and a split skin graft applied; and where the dissection was so deep that the axillary vessels were exposed, transposition flaps were used to close the defects. The mean follow up period was 3 years and one month, with a median follow up period of 2 years. Hidradenitis recurred at the site of 3 simple excisions with primary closure; a recurrence rate of 3/15 or 20%. Wide excision and skin grafting was not followed by any recurrence in the follow up period described, 46 such procedures being described. Two recurrences occurred in 9 axillae where excision and transposition flaps were used. Simple excision and closure was complicated by wound infection, haematoma and lymphangitis in one instance of each. Four of the 46 split skin grafted axillae, suffered partial graft loss (not greater than 50%); hypertrophic scars developed in 2 instances, one at a graft edge and one involving a donor site; would contracture developed in 2 instances. The complications that occurred in those axillae closed by transposition flaps included loss of the skin graft covering the flap donor site in 2 instances, haematoma formation in one instance, and scar contracture requiring surgical release in 2 instances. While excision with split skin grafting would appear superior in this series, none of the groups are comparable. In those undergoing primary closure incomplete excisions had been performed and recurrence was not surprising. While complete excisions were performed in both the skin grafting and flap groups, the extent of the disease differed between the 2 groups and this difference probably explains the higher rate of recurrence in the flap group. The measurements of the excised skin specimens were not given in this paper.

Letterman and Schurter (1974) having excised the total hair bearing area for axillary hidradenitis, recommended primary repair of the defect utilising a modified Z-plasty. They considered that this closure could be so designed as to confine scarring mainly to the axilla, to provide adequate cover of the axillary artery and vein, and to ensure effective repair of the defect with good function. No details of the number of patients treated or the outcome of such treatment in the long-term were given in this paper. Harrison (1964) described the use of posteriorly based transposition flaps to close the defect in 3 cases of axillary hidradenitis, who had undergone radical excision of the hair bearing skin. Suction drainage was used to prevent collections under the flaps. Again, no details of the outcome of treatment were given in this paper. Armstrong (1965) treated 59 cases of axillary hidradenitis between 1930 - 1963. Following excision of the involved axillary skin, the defect was covered with a split skin graft in the early years of the series, involving, in the author's words, "cumbersome and uncomfortable immobilisation". In the latter part of the series, posteriorly based rotation flaps were used. No details of the extent of excision, or recurrence rate were given in the paper. O'Brien, Wysocki and Anastasi (1976) advocated the use of an anteriorly based rotation flap in the female and a posteriorly based flap in the male, following excision of the diseased area. While measurements of the extent of excision were not given, the photographs reproduced in the paper suggest that the excisions were small in size. Seventeen axillae in 9 patients were treated with the above flaps. The procedure was well tolerated and the average post-operative stay was 3.5 days. All patients had a full range of shoulder movement by the end of the 4th post-operative week. Four of the 17 axillae developed complications, 2 had superficial epidermal necrosis at the apices of the flaps and 2 suffered separation of the wound edges at the points of maximum tension. All completed healing by secondary intention, by the end of the 3rd post-operative week. No complete flap loss occurred. The authors claimed good results for the procedure, but as no details of long-term follow up were given in their papers, this is difficult to assess.

Lipshutz (1974) completely excised the hair-bearing area of the axilla; then used 2 triangular flaps constructed from the dog ears at the ends of the wounds and based on subcutaneous pedicles, for advancement to the centre of the wound, so making good the defect. No details of the number of patients treated, or the outcome of such treatment on follow up were given in the paper.

Pollock, Virnelli and Ryan (1972) excised all grossly visible disease in 10 consecutive patients with bilateral axillary hidradenitis. Appropriate systemic antibiotics were commenced pre-operatively and continued post-operatively for 10 days. The excised skin measured 15 by 8 cm. in the contracted specimen on average. Having excised the diseased skin, the skin edges were undermined between the dermis and the subcutaneous fat for a distance of 3 mm. The wound was then closed primarily, with 8 - 16 Number One nylon retention sutures, placed 4 cm. from the wound edges, 4/0 nylon vertical mattress sutures to obtain eversion in the central portion and finally a 2/0 nylon subcuticular suture. No drains were used and the retention sutures were tied over a bolus dressing at the end of the procedure. The bolus dressing and the retention sutures were removed on the 4th day; the mattress sutures on the 5/6th day and the subcuticular suture after the 14th day. Wide arm abduction by the patient was not allowed until the 17/18th day and active stretching exercises were commenced from the 21st post-operative day. These were continued until 180° of abduction was obtained, usually by 6 weeks (range = 4 - 9 weeks). Of the 20 wounds 60% healed primarily, having no open areas at 7 days. Skin healing was delayed in 35%, with areas of serous drainage; healing was completed by the 18th day in these cases. Significant central breakdown occurred in one wound (5%). There has been no recurrence of hidradenitis at a follow up of 6 weeks to one year. Tasche, Angelats and Jayaram (1975) started to use the Pollock operation as described above in 1972. Prior to that year from 1963 to 1971 they had performed a variety of procedures for axillary hidradenitis:- Z-plasty, small excisions with primary closure following undermining of the wound edges, rotation flaps, primary split skin grafting, and delayed split skin grafting. Larger excisions were performed for the Pollock procedure, 52 cm^2. on average, with a lower recurrence

rate than that obtained by the method of primary closure in use at that time. The prolonged pre-operative hospital stay prior to 1972 was attributed to the strenuous attempts made to reduce the degree of inflammation prior to surgery, an exercise not felt necessary in relation to the Pollock procedure. The Z-plasty procedure was not found to be successful. Rotation and transposition flaps were considered to have worked well, but when they failed a long period of time was required for secondary healing and regrafting. Split skin grafting was not considered very successful and delayed grafting was not successful when tried. Tasche et al. made the point that in addition to achieving a lower recurrence rate, a higher rate of primary healing and reducing the duration of hospital stay, as compared to the other methods, the Pollock method also facilitated the treatment of both axillae at the same operation, an important consideration when the axillary involvement is bilateral in 75% of cases.

Anderson and Perry (1975) also used primary closure following excision of the hair-bearing area for axillary hidradenitis. Measurements of the size of excisions carried out, were not given in the paper. The patients were instructed to limit their shoulder movements for 2 weeks post-operatively; following which abduction to 45° was permitted, which was gradually increased to 90° at one month and to 180° at 6 weeks. This technique was used in 26 patients; 47 axillae being so treated. Post-operative problems were reported as being minor, consisting of minimal wound separation in 8 axillae, which healed spontaneously. Shoulder movements in all cases equalled or exceeded the pre-operative range within 6 post-operative weeks. Again, no details of the results obtained on long-term follow up were given in this paper. Bell and Ellis (1978) reported on the surgical management of 20 patients with axillary hidradenitis. The majority of these patients were treated by excision and primary closure; the wounds being drained in the majority of these cases. Two patients underwent excision and split skin grafting and one patient excision and spot skin grafting. The patients were followed post-operatively for a period ranging from one to 97 months, with a median follow up of 9 months and a mean of 18.75 months. One recurrence occurred in the primary closure group at 22 months.

The treatment of hidradenitis involving the groins, perineum, perianal area, pubis and external genitalia is even more problematical than that of the axilla. Newell, Voelter and Mullins (1973) advocated exteriorisation of hidradenitis tracks, followed by curettage of the tracks and electrocoagulation, apart from those lesions situated in the pararectal region. They carried out this procedure in several hundred cases, but again omitted to give their results on long-term follow up. Barron (1970) had described a similar technique and found that the dead tissue usually sloughed off in 7 - 10 days with the appearance of healthy granulations. Complete healing usually occurred in 4 weeks to 2 months, but deeper areas could take longer. The extensive scars were at first firm and prominent, but in 6 - 12 months they became soft and pliable. No details of patient numbers, or the recurrence rate on follow up were given in the paper. Adams and Haisten (1972) also tried the above technique but found healing by granulation unsatisfactory and had to resort to split skin grafting.

Thornton and Abcarian (1978) treated 104 patients with hidradenitis of the perineum or perianal area by wide excision of the involved area down to normal fat or fascia using electrocautery. The wounds were packed with iodoform gauze and an occlusive dressing applied. Skin grafts were not routinely used. The dressing and pack were removed on the first post-operative day; the patient ambulated and Sitz baths at a frequency of at least 4 times per day commenced. The wounds were allowed to heal by secondary intention with frequent Sitz baths and changes of dressing. The patient was discharged as soon as he was afebrile, comfortable and able to care for the wound, and followed up in the outpatient department twice weekly, until wound healing was complete. The average hospital stay was 7.2 days, with 80% of the patients discharged by the 10th post-operative day. Patients of more than 40 years of age required an average hospital stay of 18.7 days. The sizes of the wounds as recorded on the pathology reports were arbitarily assigned to one of 3 groups:- small (2 by 2 cm.), medium (2 - 5 by 2 - 5 cm.), or large (more than 5 cm. in any dimension). The average healing time ranged from 3.5 weeks for small wounds to more than 7 weeks for large ones. There were no deaths in the series, but 4 patients

required re-operation for recurrent hidradenitis during the 5 year period of the study. Routine antibiotics and skin grafting were not used in these patients and Thornton and Abcarian concluded that rapid healing with excellent results could be obtained by leaving the perineal wounds open to heal by secondary intention. Wound contractures were minimal and the healed perineums were pliable and non-tender. Ariyan and Krizek (1976) treated 3 cases of chronic recurrent inguinal and perineal hidradenitis by aggressive wide excision of all the involved tissue and allowed the defects to heal by secondary intention. The excisions were performed in an elliptical fashion, directed along the skin folds, and did not extend below the deep fascia, in order to provide some protection for the testis and vas deferens. No undermining of the wound edges were performed, and the wounds were then packed with saline soaked gauze. Frequent dressing changes were performed and early ambulation encouraged. The patient was discharged between the 10th - 21st post-operative day, as soon as he could manage the dressings personally and good granulation tissue was present. The wounds were usually apposing and superficial within 4 weeks and completely epithelialized by 6 - 8 weeks. The inguinal wounds healed with a linear scar and the authors made the point that while the wounds heal by contraction, wound contracture did not occur. Again, no details of the outcome of this treatment on long-term follow up were given in the paper. Vickers (1975) reported a similar management of 5 patients with scrotal and perineal hidradenitis, healing occurring by granualtion. He reported that epithelialization was complete 4 weeks post-operatively and wound contracture minimal. The average hospital stay in this series was 12 days and the average time lost from work was 3 weeks. A zero recurrence rate was claimed but no details of the length of follow up were given. Jackman (1942) believed excision of the diseased tissue and plastic repair of the defect to be the optimal management of chronic hidradenitis, but considered that in the case of perinanal and perineal disease, the wounds should be left open and allowed to heal by granulation. Between 1936 - 1942, he treated 11 patients with perianal/perineal disease and scrotal or inguinal disease in this fashion. Recurrence occurred in one case adjacent to the previous excision scar. Jackman went on to say that where

the denuded area was extensive, skin grafting, either split skin grafting or full thickness pedicle grafts could be necessary. No details of the length of follow up or measurements of the extent of excisions performed were given in the paper.

Ching and Stahlgren (1965) established the use of a diverting colostomy in the treatment of perineal/perianal hidradenitis. Prior to excision of the disease, a diverting colostomy was established. When the colostomy was working satisfactorily, the lesions were sidely excised and split skin grafting carried out secondarily. This method was used in 6 cases but detailed results of the treatment were not given in the paper. Adams and Haisten (1972) reported a similar method; they performed a diverting colostomy in 5 cases of severe perianal and gluteal hidradenitis, followed by wide excision of the diseased tissue and closed the defects by means of split skin grafts. The authors state that they obtained good results, the only complication being that one case developed anal incontinence for 6 weeks following closure of the colostomy. However, details of the results were not given. Other authors who have made use of diverting colostomies prior to excision and skin grafting of perianal disease include Moschella (1966), Hyland and Neale (1976), Chalfant and Nance (1970), Knaysi, Cosman and Crikelair (1968). Hyland and Neale (1976), in addition, used porcine xenografts to cover the perianal area, following wide excision, prior to secondary grafting of the area.

Anderson and Dockerty (1958) recommended that the defect resulting from excision of hidradenitis be closed either primarily or by split skin grafts, except in the case of the perianal area, where the wound should be left open to heal by granualtion. They treated 64 patients with perianal and perineal hidradenitis of whom 26 were lost to follow up, leaving 38 assessable patients. Of these 38 patients, 45% required further surgical treatment for hidradenitis; 32% had mild post-operative hidradenitis not requiring further surgery and 21% had no recurrence at 8 years follow up.

Ward, Washio and David (1974) describe a case of extensive hidradenitis involving the scrotum, perineum and perianal area. Both

the urinary and gastro-intestinal tracts were investigated and found to be normal. A suprapubic cystostomy was performed and the diseased scrotal and perineal tissues excised including a bilateral orchidectomy. The disease extended down to the perineal membrane but not deep to it. Their limits of excision were the peno-scrotal junction anteriorly, the anal canal posteriorly, the ischio-pubic rami laterally and the external inguinal rings superiorly. An indwelling Foley catheter was inserted to facilitate indentification of the urethra. Primary closure of part of the wound was possible but the central area of the perineum could not be closed primarily and following a period of granulation was secondarily skin grafted.

Masson (1969) considered primary closure to be suitable for the groin and upper thigh on occasion but where important structures such as the testes or large vessels were left exposed, he considered cover with pedicle grafts to be more suitable. Epithelialization was considered suitable for the nape of the neck, the scalp and the perianal area. Masson suggested that delayed free grafts be used for large defects involving the buttocks, perineal or inguinal regions.

Cocke (1967) used a combination of primary closure and free grafting for inguino-perineal disease. Bell and Ellis (1978) found that most moderately severe cases of inguino-perineal hidradenitis could be managed successfully by excision and primary closure which was used in 8 cases or by split skin grafting which was used in one case.

Thornton and Abcarian (1978) compared their method of excising perineal and perianal hidradenitis with healing by secondary intention with Ching and Stahlgren's method of a diverting colostomy prior to excision of the diseased area followed by delayed skin grafting. They found, contrary to Ching and Stahlgren's recommendations, that a diverting colostomy was necessary in only one of their patients. They also considered that primary closure and skin grafting were inappropriate techniques in the perineo-perianal area due to the contaminated nature of the wounds.

Finally Culp (1983), in his paper on perianal hidradenitis, stated that the keystone of successful management was complete exposure of the entire lesion, with preservation of the floor of the track for its epithelial regenerative elements. The unroofing of the base of the affected area should include a rim of normal appearing tissue. Thirty patients (30) were treated in this manner, with a follow up period of one to seven years. Two patients died during this period from causes other than hidradenitis and one was lost to follow up. None of the remaining 27 patients had recurrence locally but 2 developed further lesions of hidradenitis elsewhere. Preliminary diverting colostomies were not found to be necessary.

CHAPTER II

REVIEW OF THE LITERATURE ON THE APOCRINE SWEAT GLANDS

CONTENTS PAGE

CONTENTS PAGE

2.1 HISTORICAL

The sweat glands were first discovered by Purkinje in 1833 and described by his pupil Wendt. Krause (1844) first observed that the glands in the axilla, the external auditory meatus, the circumanal region, and the eyelids were larger than the other sweat glands. The large apocrine sweat glands of the axilla were clearly described and recognised to be different from the general sudoriparous glands by Horner (1846) and Rolin (1846). Kolliker (1853) described the histology of these glands. Krause (1876) was of the opinion that the ceruminous, axillary, tarsal and circumanal glands were of the same type. Ranvier in 1887 differentiated the 'holocrine' secretion of the sebaceous glands, from the merocrine secretion of the sweat glands. Schiefferdecker (1922), further classified the merocrine glands into two subclasses, the apocrine and the eccrine glands.

2.2 LOCATION

Apocrine glands have been described in a number of regions. Ellis (1967) described the apocrine glands as being present in the axilla, areola, pubis, perianal region and the external auditory meatus. Krause (1844) described the ceruminous glands as apocrine. Montagna (1962) included the nipple areola, eyelids, prepuce and scrotum as normal sites for the glands. He also included the labia minora but not the labia majora. Hewer (1969) however, included the labia majora but not the minora. Vohwinkel (1931) described the presence of apocrine glands in the skin of the forehead. Montagna and Yun (1972) later called into question the existence of any apocrine glands in the areola, nipple and breast of the female. Hurley and Shelley (1960) included the whole of the female external genitalia as sites of common occurrence, also the region over the inguinal ligament, parts of the trunk (in particular the area around the umbilicus), and the hairy regions of the male chest. Pinkus (1958) described glands occurring anywhere on the abdomen, bearded part of the face and the scalp. Homma (1926) thought that the apocrine glands could be found anywhere that hair had occurred at sometime in life, and therefore it was only in the skin of the

palms and soles that they were never found. Clee (1975) reported the finding of apocrine sweat glands in the eyebrow and nasal vestibule.

2.3 ANATOMY AND HISTOLOGY

The apocrine gland has been described both as a compound tubular gland (Woollard 1930) and as a simple tubular gland with shunts and diverticula, (Hurley and Shelley 1960). A single duct proceeds from a coiled glandular portion to open either into a hair follicle or onto the adjacent skin surface, (Hurley and Shelley 1960). Woollard (1930) believed the extra-follicular ducts to be in the majority. Clee (1975) described some of the diverticula, especially in the axillary region as being so complex as to lend support to those who describe the glands as compound tubular. He makes the further point that the distinction between a tubule being said to have a long diverticulum and that tubule dividing is an academic one.

The glandular portions of the glands lie mainly in the dermis, but when the glands are large, as is often the case in the skin over the axilla and mons pubis, they may extend deep into the subcutaneous fat, as much as 5 mm. below the surface, (Montagna and Parakkal, 1974). Horner (1846) described the apocrine glands as measuring as much as 2 mm. at their maximum diameter. Hurley and Shelley (1960) described them as being visible to the naked eye in the reflected deep dermis or subcutis as small yellow or reddish-yellow, globular masses with an average diameter of 1 mm. The reddish tint was considered to be due to their iron content.

2.3.1 THE SECRETORY SEGMENT

The histological appearance of the apocrine glands is characteristic. The secretory cells appear to be losing the apical tip of the cell histologically and this led to the belief that their secretion was formed by a process of decapitation. This resulted in the term apocrine, 'apo' being a Greek word meaning 'from' and intending to imply that part of the cell is lost in the formation of its secretion.

Pinched off luminal tips of the tubular cells are not seen in the eccrine sweat glands as described by most authors. However, Kuno (1956) has described eccrine secretory cells showing such changes in the Japanese. Hurley and Shelley (1960 p.13) quote a personal communication from O'Brien referring to an 'intermediate' gland in some biopsies he had studied which showed both apocrine and eccrine characteristics.

Apocrine sweat gland tubules possess a single type of secretory cell surrounded by a basement membrane with interposed myoepithelium. The shape of the secretory cell, however, may be cuboidal or columnar (Montagna and Parakkal 1974) and occasionally almost squamous (Montes, Baker and Curtis 1960 and Winkelmann and Hultin 1958). Hurley and Shelley (1960) state that there is no uniformity of cell height within an individual, a skin area or a single gland tubule, and that variations in cell height were evident in nearby cells within the same tubule. Clee (1975) found the height of the lining epithelium of the secretory segment to be remarkably constant within each individual gland, but extremely variable from one gland to another even within the same skin section. Slight variations were seen in some glands but these were usually only from squamous to cuboidal without apical cytoplasmic caps and from low columnar to high columnar, and any variation was confined to small patches of epithelium. He also found that no particular type of gland was characteristic of any one region as glands ranging from squamous to high columnar were of widespread distribution, apart from in the small sample he obtained from the labium majus, where all the glands seen in his study were columnar. However, it did appear to Clee (1975) that there were two very contrasting appearances which the apocrine glands could assume and that both of these contrasting types were commonly seen in any one region at any particular time. He describes these two contrasting types as (1) squamous or cubical without apical cytoplasmic caps, and (2) high columnar with large, well formed apical cytosplasmic caps on virtually every cell. Linking these histological findings, with physiological and pathological evidence, Clee (1975) postulates a theory for the secretory cycle of the apocrine gland and this will be discussed below in the physiology of the apocrine glands.

The apocrine secretory cells are eosinophilic, and have one or two large spherical nuclei which are basally located. The nuclei are round and stain deeply with basic dyes and the Feulgen reaction. They possess one or two large nucleoli flanked by two strongly basophilic, Feulgen-positive satellite bodies (Montagna and Parakkal, 1974). The bases of the cells have a highly folded villous nature with folds of adjacent cells inter-twining; filling the gaps in the layer. The luminal borders of the cells possess cytoplasmic caps from which microvilli protrude, and a brush border (Minamitani, 1941, and Montagna, Chase and Lobitz, 1953) consisting of a fringe of minute microvilli covering the free surface of the apical cytoplasm. The luminal border also shows a fringe or row of what appears to be tiny droplets, first described by Montagna, Chase and Lobitz (1953) and was thought to represent apocrine secretion. Montes, Baker and Curtis (1960) failed to confirm this finding.

2.3.2 THE DUCT

Hurley and Shelley (1960) state that the ductal portion of the apocrine gland is difficult, if not impossible, to distinguish from that of the eccrine gland on histologic appearance alone. They describe the apocrine duct as having a double layer of basophilic cuboidal cells, being devoid of myoepithelium and possessing a well-defined basement membrane. The apocrine duct is described as being of larger calibre and more eosinophilic than the eccrine duct, and the transition from tubule to duct as being abrupt. The intra-epidermal end of the duct is marked by the presence of a luminal hyaline fringe, the cuticle, which is also visualised at the same level in the eccrine duct. The intra-epidermal portion of the apocrine duct is described as straight and not coiled, as is the eccrine duct. Keratinisation near the open end of the apocrine duct is also described. Hurley and Shelley describe the duct as becoming funnel-shaped at its upper end (the infundibulum) and opening into the hair follicle above the sebaceous ducts or onto the skin surface. Up to three ducts opening into a single follicle have been observed. Montagna (1962) stated that the upper part of the secretory segment, which has a diameter less than one-third of that of the lower coils, became abruptly attenuated

and merged into a narrow duct, which had a relatively straight course, running roughly parallel to the hair follicle.

Ellis (1967) described the duct of the apocrine gland as being a typical sweat gland duct consisting of two concentric layers of cubical cells, the terminal cells having a poorly developed cuticular border (a meshwork of tonofilaments). Hashimoto, Gross and Lever (1966) described the ultrastructure of the duct and confirmed many of the previously noted features, but described several new features, one of which was that the apocrine duct had a trilaminar wall. Charles (1959) had noted some duct profiles lined by three layers of cubical cells, but did not advance this as the rule. Hashimoto, Gross and Lever (1966) felt that the eccrine and apocrine glands could be distinguished by their ducts alone, the latter having three concentric layers and the former only two. Montagna and Parakkal (1974) described the duct wall as having two layers. However, they describe the terminal funnel shaped part of the duct as multi-layered, and also describe the presence of myoepithelial cells about the duct.

Clee (1975) in his work on the apocrine gland, was not able to reach any firm conclusions on the duct structure. The majority of ducts visualised were bilaminar and lacked a myoepithelium, but he also visualised a number of ducts which exhibited a trilaminar stratified cubical epithelium and in some ducts a layer of myo-epithelial nuclei was thought to be present. In an attempt to explain the disparity in the findings of the various workers, he advanced the following possibility: the myoepithelium of the secretory segment may extend for a variable distance up the duct and that in the more superficial parts of the duct extra layers may be present on the exterior of the duct possibly originating from the cells of the hair follicle, which in between, a simple bilaminar appearance without a myoepithelium exists.

These disparities in apocrine ducts architecture do not facilitate the distinction of apocrine from eccrine sweat gland by duct alone.

2.3.3 MYOEPITHELIUM

The apocrine sweat gland possesses a well-developed band of cells which closely invests the tubular portion of the gland and which possess many of the properties of smooth muscle - the myoepithelium. The myoepithelial cells are spindle-shaped, 4 - 6 u in diameter and 40 - 100 u long, lying with their long axes parallel to that of the tubules and are lodged in grooves between the bases of the secretory cells. Thus secretory cells and myoepithelium rest alternatively on the basement membrane. Hurley and Shelley (1960) described the myoepithelial cells as being better developed in the apocrine glands than in the eccrine glands but not as prominent as in the breast. The cytoplasm of the myoepithelium stains strongly with acid dyes such as eosin,but especially well with phosphotungstic acid haematoxylin and the PAS reaction (Bunting Wislocki and Dempsey 1948; Hurley and Shelley 1960). Phosphotungstic acid haematoxylin stains deep blue the numerous longitudinal fibrils dispersed throughout the cytoplasm which are more numerous and coarse than the myofibrils demonstrable by the same method in the smooth muscle cells of arterioles and arrectores pilorum muscles (Bunting et al. 1948). Bunting found bifringence to be present in the myoepithelial cells which was not extracted with acetone or pyridine. Schmitt (1944) demonstrated positive bifringence with respect to the long axes of the myoepithelial cells, with first order red plate, indicating the presence of longitudinally orientated rodlets or fibrils. This property is similar to that of smooth muscle in general (Fischer, 1936). The myoepithelial cells are best developed in those secretory tubules lined with columnar epithelium; in dilated tubules lined with flat elongated cells they are impossible to demonstrate (Montagna and Parakkal, 1974). Hurley and Shelley (1960) concluded that they were contractile, expelling apocrine sweat from the tubular lumen. This will be discussed further under the physiology of the apocrine gland.

2.3.4 LUMINAL CONTENTS

The lumen of the apocrine profile may contain cellular casts or debris which Hurley and Shelley (1960) state was a much more marked

feature after frozen section or freeze drying, but was still evident after routine formalin fixation. Montes, Baker and Curtis (1960) describe the luminal contents as varying from a loose stringy pattern to a compact dense mass, staining with the PAS reaction and aniline blue, the intensity of the staining being directly proportional to the density of the secretion. He adds that dense luminal contents are usually accompanied by a flattened epithelium, and that this may have resulted from blockage of the ducts with a resultant increase in intraluminal pressure. Montes, Baker and Curtis (1960) believed that some of the cellular debris may be due to degenerating epithelial cells, and that trauma at biopsy was probably the cause of the extrusion. They found nuclei and cell fragments giving basophilia to the luminal contents to be rare. Ito, Tsuchiya and Iwashige (1951) considered these to be a normal constituent of the secretion.

Montagna, Chase and Lobitz (1953) found the contents of the tubules to be clear and colourless and never found any cell debris to be present in the lumen. This was attributed to the fact that biopsy specimens rather than autopsy specimens were used in this study. They found, by serially tracing the long apparently detached cytoplasmic terminations in the lumen, that they were attached to the subjacent cells. They did agree that degenerating or cystic tubules contained debris in their lumena. However, in 1959, Montagna appeared to support Montes, Baker and Curtis (1960) in that the lumen may be full of casts of cells and cell debris, some of which may still be intact. He pointed out that these were most commonly seen in glands with a flattened epithelium.

2.4 THE AXILLA

In the human, the axilla possesses the largest and best developed apocrine glands. In addition, nowhere else in the body are apocrine and eccrine glands so intimately associated, (Montagna and Parakkal, 1974). In the vault of the axilla, nearly every hair is associated with one large gland, and they form an almost uninterrupted sheet of glandular tissue in the reticular layer of the dermis. Delineation of one apocrine gland from another in this region is difficult, in that the glands are crowded together, often masking the connective

tissue barriers that separate them. They may also extend beyond the dermis into the subcutis (Woollard, 1930). In Down's syndrome and other forms of mental deficiency, axillary hair is often absent and this is accompanied by underdevelopment or absence of axillary apocrine sweat glands (Shelley and Butterworth, 1955).

2.5 PUBIC REGION

Homma (1926) studied sections of skin taken from the breast; from halfway between the umbilicus and the symphysis; from the mons pubis and the region around the anus. He concluded that in those specimens examined the apocrine glands were most common in the pubic area. Woollard (1930) removed strips of skin from the axilla, the mammary region, the pubic and circumanal region, of the formalinised cadavers of two mature Aboriginal males. Large apocrine glands, in addition to eccrine glands were found in the axilla and circumanal region in both cases. In the pubic and mammary areas, groups of glands were met in which the lumen was slightly larger than in the case of eccrine glands. In some such glands the lumen was filled with coagulated material and desquamated cells. In some cases they gave a positive iron reaction. These glands he classified as apocrine. He found 12% of 104 sections sections taken from the pubic region to contain apocrine glands, in comparison to an apocrine gland population in the axilla and circumanal region so numerous that no figures were given.

In 1964, Kligmann and Shehadeh studied the physiology of the apocrine glands in the pubis in connection with their non-odorous properties. (They describe the distribution of apocrine glands in this region as genito-inguinal). As the work of Hurley and Shelley (1960) and their own work (Shehadeh and Kligmann 1963) had demonstrated that axillary odour was due to the breakdown of apocrine sweat by bacteria, they initially compared the resident bacterial flora of the axilla and pubic area. They appeared satisfied that while bacterial counts were lower in the pubic region than the axilla, this difference did not contribute to the lack of pubic odour. Trials of local injections of both cholinergic and adrenergic agents convinced them of the total unresponsiveness of the pubic area

to either form of physiologic stimulation; nor could apocrine droplets be milked manually. They found the histological and histochemical properties of the pubic apocrine glands to be identical to those of the axilla; but the pubic apocrine glands were smaller. It was concluded that the pubic apocrine glands were anatomically perfect but physiologically functionless.

Clee (1975) studied 6 blocks of skin from the suprapubic region of 3 individuals. He found apocrine glands to be present in 50% of this material. The apocrine glands were smaller than those of the axilla and shunts and diverticula were fewer. However, PAS positive material was present in the cytoplasm of the secretory cells and PAS positive material was present in the lumen. The secretory portions of the glands and their ducts were noted to be in continuity. Clee (1975) then proceeds to argue against Kligmann and Shedadeh's findings that the pubic apocrine glands fail to sweat in the following fashion: Montes, Baker and Curtis (1960) considered the presence of PAS-stained bodies within the epithelium and/or the presence of PAS positive material in the lumen of the secretory profile, was a good indication that the gland in question was involved in apocrine secretion. PAS positive material seen in the lumen of the pubic apocrine glands, suggested that apocrine secretion was being formed. Fox-Fordyce disease caused by the accumulation of apocrine sweat in obstructed ducts is not uncommon in the suprapubic region. This fact and the improvement in the condition during pregnancy, when apocrine gland function is thought to be reduced, being restored post-puerperium (Cornbleet 1952b) suggests that the pubic apocrine glands are capable of producing secretion. Chromidrosis, which is defined as the production of coloured apocrine sweat also occurs in the suprapubic region (Shelley and Hurley, 1954 and Hurley and Shelley, 1960), again suggesting that suprapubic apocrine secretion occurs.

The appearance of apocrine sweat on the skin surface (apocrine sweating), is a function distinct from the formation of the sweat itself (apocrine secretion) in the secretory tubules (Hurley and Shelley, 1960). Clee (1975) noted that the suprapubic apocrine ducts were in continuity with the hair follicles, and that a well-

developed myoepithelium was present. Kligmann and Shehadeh (1964) themselves noted innervation of the suprapubic apocrine glands. These factors suggest that the mechanism by which apocrine secretion is delivered to the skin as sweat, is intact in the suprapubic apocrine glands. Clee (1975) points out that in the presence of suprapubic apocrine secretion, Fox-Fordyce disease and hidradenitis suppurativa would occur throughout the population, if the suprapubic apocrine ducts were not in continuity with the hair follicles or skin surface, or if those ducts were not patent.

Apocrine sweat is odourless when it appears on the skin surface of the axilla and only acquires the characteristic axillary odour after it has been acted upon by the bacterial population of the axilla (Shelley, Hurley and Nichols, 1953 and Hurley and Shelley, 1960). In addition, according to Hurley and Shelley (1960) the axilla is the perfect site for harbouring the maximal resident population of bacteria. Clee (1975) advances the following possible reasons for the lack of odour in the pubic area (a) the suprapubic apocrine glands are smaller and more scattered than those of the axilla, resulting in a decreased amount of apocrine sweat, (b) the bacterial counts are lower in the pubic area than the axilla, (Kligmann and Shehadeh, 1964), (c) the relative proportion of eccrine glands to apocrine glands is higher in the pubic area than the axilla, resulting in apocrine sweat being washed away by eccrine sweat and preventing odour formation (Shelley, Hurley and Nichols, 1953).

2.6 THE CIRCUMANAL GLANDS

Homma (1926) studied 129 sections of circumanal skin from 11 white people and found apocrine glands in 7% of the sections, and 179 sections of the same region in 12 coloured people, finding apocrine glands in 53% of these sections. He considered the frequency of apocrine glands in the areas he examined to be, in decreasing order:- the axilla, mons veneris, the circumanal skin, the abdominal skin and the breast. Woollard (1930) felt that the apocrine glands were found abundantly in only two regions, the axillary and circumanal regions. Homma (1926) described the anal glands as occurring

about 15 mm. from the anal margin where they formed an oval ring of approximately the same width. The individual glands were described as being three times the size of eccrine glands in the same region. Woollard (1930) described large circumanal apocrine glands in two Aboriginal subjects extending throughout sections 2 - 5 cm. wide, the glands being of similar size to those in the axillary organ. Woollard (1930) suggested that Homma (1926) missed the circumanal apocrine glands in his study on the Caucasians.

Clee (1975) found apocrine glands in 33% of the blocks of circumanal skin examined and typical apocrine glands in 75% of blocks obtained from the labium majus.

2.7 THE BREAST

Bunting (1948) reported the presence of structures in the human mammary gland which resembled apocrine sweat glands. He described them as being lined by tall columnar eosinophilic epithelium and often being cystic or having papillary growths. They are said to be within the lobules of the breast and to be connected with the lactiferous ducts (Lee, Pack and Scharnagel, 1933; Cheatle and Cutler, 1931), unless they are cystic when no such connections are demonstrable (Foote and Stewart, 1945). Other investigators (Dawson, 1932; Goldzieher and Kaldor, 1930; Geschickter, 1945) believed the altered appearance of the mammary epithelium to be the result of degenerative changes, and the resemblance to apocrine sweat glands purely fortuitous.

Montagna and Yun (1972) serially sectioned the human female nipple, and considered the areolar tubercles to be the sites of the ducts of Montgomery's glands and sebaceous glands. They were unable to find any apocrine glands in the nipples.

Giacometti and Montagna (1962) pointed out that, although the mammary glands are said to be 'modified' apocrine sweat glands, the two have neither gross nor histological and histochemical resemblances (Fanger and Barker 1960). Giacometti and Montagna concluded that the available evidence did not constitute proof against the concept

that mammary tissue is a modified apocrine sweat gland, but that if it was, any resemblance between the two had been lost.

2.8 INNERVATION

The State of innervation of the apocrine sweat glands is uncertain.

Woollard (1930) stated that the apocrine glands were supplied by neurofibrillae which ended on the basement membrane. The secretory cells were without demonstrable innervation. Cahn and Shelley (1955) demonstrated neurofibrillae around the periphery of apocrine gland secretory tubules in human male axillary skin, with both methylene blue and silver stains. Thies (1958) found that neither the apocrine nor eccrine ducts have any form of innervation but Charles (1959) reported non-medullated nerve fibres in the walls of apocrine ducts in an electron microscopic study.

However, it is still not firmly established what is the exact nature of the nerve supply of the apocrine gland. Shelley and Hurley (1953), Thies and Galente (1957), Montagna and Ellis (1958) and Hurley and Shelley (1960) failed to demonstrate the presence of nerves giving a positive cholinesterase reaction in the immediate vicinity of the apocrine glands. According to Beckett, Bourne and Montagna (1956) the eccrine sweat glands are surrounded by nerves rich in specific cholinesterase activity, from the time they are formed in the fourth foetal month; but apocrine sweat glands never show such nerves around them.

Hurley and Shelley (1960) stated that the innervation of the human apocrine sweat gland is derived from adrenergic fibres of the autonomic nervous system. The nerve fibres were poorly demonstrated by silver stains, and they found it difficult to determine the precise site of termination of the nerves. The myoepithelial cells appeared to be innervated, but they were unable to ascertain whether the secretory elements were innervated. Shelley, Cohen and Koelle (1955) were unable to demonstrate nerve fibres showing monoamine oxidase activity.

Utilising the cholinesterase technique of Koelle (1951), at the usual incubation times of 30 and 120 minutes, Hurley, Shelley and Koelle (1953) demonstrated an absence of specific cholinesterase about apocrine sweat gland tubules, also an absence of non-specific cholinesterase suggesting that the apocrine glands were not supplied with cholinergic fibres. If they continued the incubation times of Koelle's cholinesterase technique to 4 hours or beyond, some of the fibres were stained. However, they state that the staining was incomplete and this was consistent with the very low concentrations of cholinesterase present in adrenergic fibres.

Perry et al. (1955) using silver stains demonstrated the presence of fine argyrophilic fibres around many of the ceruminous gland tubules in the human external auditory meatus. These they interpreted as nerve fibres. Stains for specific and non-specific cholinesterase did not reveal evidence of these enzymes around the ceruminous glands. Control specimens taken from the arm showed abundant specific cholinesterase about the eccrine sweat gland tubules. Perry et al, suggested that the nerve fibres about the ceruminous glands were adrenergic motor fibres of the autonomic nervous system. Robertshaw (1974) presented evidence that the apocrine glands in several species are controlled by adrenergic nerves and by circulating catecholamines of adrenomedullary origin.

Rothman (1954) and Aavik (1955) have reported and illustrated cholinesterases around human axillary apocrine glands. Montagna and Ellis (1960a) reported that the axillary apocrine glands of the Negro have variable numbers of cholinesterase-positive nerves around them, but those of Caucasians do not: however, in a later paper Montagna (1964) states that although not as prominent as in the Negro, the axillary glands of Caucasians may also be surrounded by cholinesterase containing nerve fibres. This agreed with the pharmacological studies of Aoki (1962). Montagna (1964) also demonstrated conspicuous nodules along the cholinesterase-containing nerves of the axillary skin. Montagna and Ford (1969) reported the glands of Moll in the eyelid as having cholinesterase-positive nerves about them, and Kligmann and Shehadeh (1964) demonstrated the presence of specific cholinesterase in a rather sparse network

of nerves about the secretory portions of pubic apocrine glands. With some exceptions, the apocrine glands over the general body surface of many primates have no cholinesterase-containing nerves around them. (Montagna and Ellis, 1959, 1960b; Montagna 1962). The apocrine glands in specialised skin areas in many primates are, however, rich in cholinesterase containing nerves. Such nerves are also found around the axillary apocrine glands in chimpanzees and gorillas; in the glands of the antebrachial organs of ring tail lemurs; around those of the brachial organs of the lorises, and the body glands of the horse (Montagna and Parakkal 1974). Montagna (1964) has also demonstrated that the nerves around both types of sweat gland, the hair follicles and blood vessels in the axilla contain a trace of butyrylcholinesterase.

Rechardt et al. (1976) utilised formaldehyde-induced fluorescence to study adrenergic nerves and thiocholine techniques to demonstrate cholinergic nerves at the light and electron microscopic levels, in specimens of axillary skin obtained from hyperhidrotic and normal patients. No fluorescent nerves (adrenergic) were found around eccrine or apocrine glands in hyperhidrotic or normal sweating axillae. Both eccrine and apocrine sweat glands exhibited a nerve network showing acetylcholinesterase activity. The acetylcholinesterase positive nerves were not seen to penetrate the basement membrane.

2.9 BLOOD SUPPLY

Ellis, Montagna and Fanger (1958) utilised an azo-dye technique for alkaline phosphatase to outline the vascular supply to the apocrine glands. The apocrine glands studied were in skin obtained from the axillary organ and the external auditory meatus. The capillaries supplying the apocrine glands emerge from adjacent arterioles. The capillaries form elaborate systems of loops and interconnecting branches, bifurcations and cross shunts around the tubules. The vessels adhere to the surfaces of the tubules but they were never seen penetrating their surface. There was no apparent difference in the blood supply to the dilated or the constricted segment of the tubules, each being supplied with an

equal number of capillaries. A few capillaries followed the duct of the apocrine gland to its junction with the piliary canal.

Hurley and Shelley (1960) describe the secretory portion of the apocrine sweat gland as being supplied by small arterial branches from the deep dermal arterial plexus. Tiny arterioles which partially envelop the tubules break up into small capillaries. The venules follow the course of these vessels and ultimately drain into the deep dermal plexus of veins. They describe a small arteriole and venule following the apocrine duct as it progresses upward, as in the eccrine duct. The arterial supply to the axilla is derived from branches of the subscapular and anterior circumflex humoral arteries, the axillary artery itself and from the intercostal arteries. Tributaries carry the venous blood from the deep dermal plexus of veins into the axillary vein.

2.10 LYMPHATIC DRAINAGE

Lymphatic drainage is via a plexus of vessels in the dermis just deep to the vascular plexus. In the axilla the lymph goes to the axillary nodes and then via large lymph vessels to the thoracic and right lymphatic ducts (Hurley and Shelley, 1960).

2.11 PHYSIOLOGY AND PHARMACOLOGY

Hurley and Shelley (1960) divided apocrine sweat gland function into 2 distinct phases:-

Apocrine sweating - the appearance of apocrine sweat on the skin surface.

Apocrine secretion - the actual formation of the sweat in the secretory tubules.

2.11.1 APOCRINE SWEATING

Apocrine sweat usually appears at the hair follicle orifices. Hurley and Shelley (1960) noted a fairly large number of apocrine sweat droplets appearing at extra-follicular sites, in some people.

This was more common in White subjects and was never more than 1 - 2% of the total number of droplets seen. The sweat is usually visualised as a turbid white fluid, but may show a yellowish tint, and rarely be blue, green or black in colour. It is commonly translucent but may vary from clear to turbid,the latter particularly occurring in the Negro. The quantity of sweat which appears at a given follicle is small (0.001 ml. per gland), but the Negro is said to produce relatively greater amounts.

Newly-expelled apocrine sweat appears as a viscid, globular droplet, but dries quickly, forming an adherent, glistening, glue-like residue over the follicular orifice within a few minutes. Whether dry or recently secreted, apocrine sweat fluoresces when exposed to Wood light. In general, an increase in the colouring of apocrine sweat tends to increase the fluorescence but dark blue and black sweat did not fluoresce at all (Hurley and Shelley, 1960).

After a stimulus which evokes good apocrine sweating, subsequent stimulation fails to produce further apocrine sweating for a period of 24 to 72 hours (Hurley and Shelley, 1960). This is referred to as the refractory period and was thought to represent the time required to form a new supply of apocrine sweat.

Fox et al. (1974) described a surge of apocrine gland activity in the morning which was maintained into the afternoon, then diminishing through the evening to reach a minimal level overnight. They described the glands as emptying independently of one another and of variable intervals between gland discharge.

Rothman (1954) suggested that the apocrine glands were capable of producing 2 secretions. One typical of apocrine sweat, and the other a clear, colourless, watery fluid which emanated from the same hair follicle, in response to heat and cholinergic drugs. Atropinisation of the area will prevent the appearance of the colourless fluid. Hurley and Shelley (1960) concluded that the human apocrine gland produced only the viscid turbid white sweat. They considered the clear, aqueous follicular fluid to be eccrine sweat arising from adjacent eccrine sweat duct pores and then spilling

into the follicular orifices giving a false impression of its origin.

Hurley and Shelley (1960) found apocrine sweating could be induced by stresses which evoked fear or apprehension; by severe pain; by local deep heat and by local deep cold. Apocrine sweating was not stimulated by general heat or cold; nor was the quantity or quality of apocrine sweat influenced by seasonal variation.

Apocrine sweating was produced by local and systemic injections of adrenalin; and by local injections of nor-adrenalin. Pitocin, the oxytocic principle of the posterior pituitary was also found to be a potent stimulator of apocrine sweating.

Hurley and Shelley (1960) found that administration of acetylcholine intra-dermally failed to induce true apocrine sweating; however, follicular eccrine sweating was observed. Pilocarpine administered intra-dermally produced apocrine sweating in a minority of study subjects. Atropine failed to produce apocrine sweating when injected intra-dermally into the axilla. Subsequent introduction of adrenalin into the atropinised area produced apocrine sweating.

However, Aoki (1962) found that the human axillary apocrine glands responded not only to adrenalin, but also to cholinergic agents such as acetylcholine, acetyl-B-methylcholine and carbaminoyl-choline. The glands discharged a viscous turbid sweat, apocrine in type, regardless of whether stimulation was adrenergic or cholinergic. Atropine injected intra-dermally completely abolished apocrine or eccrine sweating in response to cholinergic agents, injected at that site. These findings are supported by those of Kligmann and Shehadeh (1964) who stimulated apocrine axillary sweating by both adrenergic and cholinergic agents.

2.11.2 THE ROLE OF THE MYOEPITHELIUM

The apocrine secretion is thought to be expelled up the duct, resulting in apocrine sweating, as a result of contraction of the myo-epithelium. Hurley and Shelley (1960) advanced the following arguments in support of this hypothesis:- (1) That light stroking

of axillary skin and locally anaesthetised axillary skin produced apocrine sweating solely in the stroked area; (2) Local deep heat or cold, produces apocrine sweating, possibly by stimulation of the myoepithelium, while generalised heating or chilling does not; (3) Square wave electrical stimulation with a needle electrode produced apocrine sweating, possibly by stimulation of the myoepithelium, and (4) The pharmacological agents which produce apocrine sweating, also stimulate contraction in other types of smooth muscle. They attempted but failed to demonstrate myoepithelial contraction in vitro, but succeeded in demonstrating contraction in vivo. This consisted of incising the axillary skin and examining the apocrine tubules under stereoscopic magnification. Peristaltic waves were observed in the apocrine tubules in response to adrenalin and oxytocin. The peristaltic waves coincided with the appearance of apocrine sweat at the skin surface.

Hurley and Shelley (1960) demonstrated that a drop in electrical skin resistance did not occur during apocrine sweating, as opposed to eccrine sweating which caused a significant drop in electrical skin resistance. These findings agreed with those of Darrow (1932) and Lobitz and Campbell (1952). It was thought that these findings supported their concept that no active cellular secretion occurred at the time of apocrine sweating, the apocrine secretion formed in the apocrine tubules being expelled at the time of sweating, by contraction of the myoepithelium.

2.11.3 APOCRINE SECRETION

The name 'apocrine' was given to these sweat glands because it was believed, on morphological grounds, that the free ends of the cells were pinched off into the lumen on contraction of the myoepithelial cells. Further studies have cast doubt upon this as the mechanism of apocrine gland secretion.

Schaumburg-Lever and Lever (1975) made an electron microscopic study of human axillary apocrine glands, and described 3 types of secretion:- merocrine, apocrine and possibly holocrine. Charles (1959) having made an electron microscopic study of the glands,

suggested that they secreted both simply through the membranes of its cells and necrobiotically by a presumed exudation of cell contents after apical breakdown of the membrane. The evidence for simple secretion was the presence of canaliculi between the secretory cells, and the protrusion of the bordering cell surfaces into delicate papillae, the purpose of which was considered to be an increase in surface area. Charles also found the surfaces of the cells lining the apocrine duct to be papillate, and thought that the papillae, together with the rich mitochondrial content of the cells and the innervation of the duct, suggested that the ducts exerted some control on the composition or concentration of the sweat. Hashimoto, Gross and Lever (1966) also made an electron microscopic study of the apocrine duct. They found breaks in the luminal plasma membranes of the duct cells adjacent to the secretory segment, through which cytoplasm was discharged into the lumen. In the upper portion of the duct near the pilo-sebaceous apparatus, secretion took place by the pinching off of microvilli.

Inque (1979) studied the human axillary apocrine glands utilising scanning electron microscopy. Three types of apocrine secretion:- macroapocrine, microapocrine and intermediate apocrine were observed. In the macroapocrine type of secretion a round projection bulged up from the surface of the secretory cell, and separated. In the microapocrine type, the tips of microvilli which covered the large apocrine projection were expanded and separated. In the intermediate apocrine type, several secretory projections were formed at the luminal aspect of the cell, as a result of coalescence of several swollen microvilli. Inque also observed the presence of small round pores on the luminal plasma membrane, and it was thought that these may play a part in merocrine secretion. In addition, secretory cells with ruptured luminal plasma membranes and exposed nuclei and cell organelles were observed, but whether or not this represented holocrine secretion was unclear.

In conclusion, it may be said that apocrine, merocrine and holocrine secretion have all been described in the apocrine secretory tubule.

2.12 APOCRINE SWEAT CONTENT

There still appears to be little known of the chemical composition of apocrine secretion/sweat.

Hurley and Shelley (1960) found the pH of axillary apocrine sweat in healthy males to vary between 5.0 and 6.5. They also produced evidence that apocrine sweat contained protein, carbohydrate, ammonia and ferric iron, the latter being variable. Histochemical studies suggested that lipids were present.

Montes, Baker and Curtis (1960) utilising histochemical techniques suggested that the secretory product was a lipoprotein. Esterly et al. (1972) and Winkelman and Hultin (1958) have demonstrated the production of mucopolysaccharides by some normal apocrine glands.

Labows et at. (1979) have demonstrated the presence of the two androgenic steroids dehydroepiandrosterone and androsterone sulphates, in human apocrine gland secretion. These steroid sulphates were characterised by the gas chromatographic/mass spectrometric analysis of the odorous steroids formed on direct injection of the apocrine secretion into the hot gas chromatographic injector. Cholesterol was found to be the major steroid component of the secretion.

Montagna and Parakkal (1974) suggested that in some cases e.g. chromidrosis, the apocrine glands may secrete chromogens, such as indoxyl, a malodorous compound, which when exposed to air, is oxidised to blue indigo, perhaps as a result of bacterial decomposition.

2.13 ODOURS OF THE APOCRINE GLANDS

Shelley, Hurley and Nichols (1953) demonstrated that apocrine sweat is odourless and sterile when it initially appears on the skin surface. Axillary micro-organisms act on the apocrine sweat to produce the typical acrid body odour within a few hours. Exclusion of these organisms or inhibition of their growth (by the addition

of hexachlorophene) prevents any odour from developing. They demonstrated that from the practical standpoint the intensive use of hexachlorophene-detergent preparations will abolish axillary odour for more than 18 hours in most persons. Shaving of the axillary hair also reduces axillary odour, as the axillary hair acts as a collecting site for axillary secretions, debris, keratin and bacteria.

Shelley, Hurley and Nichols (1953) showed that pure eccrine sweat, whether sterile or unsterile, neither had nor developed an odour. However, eccrine sweat contaminated with sebum, keratin or debris, developed an odour presumably as a result of bacterial action. The odour was mild and distinct from the odour developing in apocrine sweat. The role of eccrine sweat in the production of axillary odour was thought to be an accentuation of bacterial growth and the volatilization of the odouriferous compounds derived from the apocrine sweat.

Kligmann and Shehadeh (1964) also found the characteristic axillary odour to result from the bacterial decomposition of apocrine sweat; gram-positive species, notably coagulase negative staphylococci were responsible for this.

Rothman (1954) suggested that the skin odours belonged to the category of caprylic odours and originated from free volatile fatty acids. The purest odour, emanated from the pubic areas; the axilla being more pungent and that of the scalp milder. Rothman also considered that odorous substances were excreted by the sebaceous glands. He also drew attention to the strong axillary odour in adolescents which becomes less intense in maturity.

Kligmann and Shehadeh (1964) in determining why the pubic area lacked the characteristic odour of the axilla, concluded that there were no important differences between the axillary and pubic microflora, and that the pubic apocrine glands were anatomically perfect but physiologically inert.

Montagna and Parakkal (1974) suggested that human beings have

characteristic as well as specifically individual and topographic odours, which may play a subtle role in human communication.

However, Doty et al. (1978) using both male and female human observers, found that only a small proportion of them were able to determine the sex of male and female donors from the odour of their apocrine secretion, above chance levels. Their results supported the following conclusions; that male and female responses to axillary odours are generally similar in magnitude and direction, regardless of the donor's sex, and that the assignment of an odour to a gender is closely related to the perceived intensity and pleasantness of the odour, with the stronger and less pleasant odours being more frequently assigned to a male gender. Finally, the intensity and pleasantness of axillary odours, on average, are inversely related.

2.14 AUTOLYSIS AND DESQUAMATION

Woollard (1930) pointed out that after late fixation, extensive desquamation of the cells lining the apocrine tubules had occurred, while none had occurred in the eccrine glands seen in the same section. Homma (1926) had reported similar findings.

Clee (1975) studied apocrine glands in skin sections obtained at necropsy. It was noticed that almost all of the high columnar glands which were seen exhibited a fairly advanced degree of autolysis. In the majority of sections, glands of low columnar type exhibited an intermediate degree of autolysis. In many cases perfectly normal apocrine glands of the squamous type and eccrine glands were seen in the same sections. Autolysis was most severe in the axilla, followed by the labium majus and the circumanal region in that order. Clee speculated that the autolysis may be due to lysosomal breakdown, or to bacteria travelling down the apocrine ducts post-mortem and invading the glandular epithelium resulting in cellular breakdown. The increased autolysis in the high columnar epithelium could be explained by their richness in PAS positive granules, thought to represent apocrine secretion; a favourable substrate for bacterial action. Again, the finding that autolysis occurs most frequently in the axilla, may be explained by the suit-

ability of the axilla as a bacterial habitat.

2.15 AUTOFLUORESCENCE

Montagna (1964) reported that when fixed or unfixed frozen sections were mounted in non-fluorescent glycerin and viewed under near ultra-violet light, maximal autofluorescence was seen in the yellow or brownish pigmented granules which emitted an orange light of moderate intensity. The luminal contents were practically non-fluorescent. It was, therefore, suggested that the pigment was probably not secreted directly into the lumen except when whole cells are cast off.

Hurley and Shelley (1960) found most specimens of milky apocrine sweat droplets to fluoresce in ultra-violet light. They emphasized that eccrine and apocrine sweat could be sharply distinguished on the basis of this fluorescence, because eccrine sweat never fluoresces. Fox et al. (1974) utilised this fluorescent property of apocrine sweat to demonstrate the beads of apocrine sweat collected on plaster of Paris discs applied to the axilla. There were quantitative differences in the degree of fluorescence of the spots of apocrine sweat. It was though that this may be due to partial emptying of a gland, varying rates of emission, or more than one gland opening into a hair follicle.

2.16 CHROMIDROSIS

The pigmented granules present in the apocrine secretory cells, which include autofluorescence among their properties, belong chemically to the lipofuscin family. It is the pigment contained in these granules which is believed to be responsible for the occasional colour in apocrine sweat (Hurley and Shelley, 1960).

Apocrine sweat may be coloured in some individuals in a localised or generalised fashion. Localised chromidrosis is most common in the axilla but has most often presented clinically on the lower eyelids of young women or elsewhere on the face. Its occurrence has also been reported on the abdomen, chest and thigh. The

age range of reported cases has varied from 15 to 57 years of age, with an average of 22 years. In most cases, the colour of the sweat was black or very dark, but brown, blue and yellow have been described. The colour may appear 4 to 5 times a day and during sleep. The appearance of apocrine sweat is preceded by a pricking or warm sensation. Hurley and Shelley (1960) considered chromidrosis to be a disorder of the apocrine sweat gland, its occurrence at skin sites not generally considered to contain apocrine sweat glands being explained by the presence of ectopic apocrine glands. Hurley and Shelley found an increase in the number of lipofuscin granules in chromidrotic glands. The blue or black apocrine sweat seen in chromidrosis was found not to fluoresce.

2.17 THE DEVELOPMENT AND NATURAL HISTORY OF THE APOCRINE GLANDS

2.17.1 EMBRYOLOGY

The eccrine and apocrine sweat glands differ not only in their histological structure but also in their embryonic development; the eccrine glands developing from the free surface of the skin, while the apocrine glands take origin from a hair follicle (Homma, 1926). The apocrine glands are thus derivatives of the same embryonic tissues as the sebaceous glands and hair follicles. Between the fourth and fifth months of intra-uterine life all hair follicles have the potential to develop apocrine sweat glands (Hurley and Shelley, 1960). The embryonic development of the glands has been reviewed by Montagna and Parakkal (1974). Each primordial hair follicle in the axilla, when already well-formed late in the 5th foetal month, has three characteristic humps on the side where it forms an obtuse angle with the surface. The lowest is the bulge to which the arrector pili muscles will become attached and the middle (the largest) will differentiate into the sebaceous glands. The uppermost hump is the primordium of the apocrine gland. The rudiments are substantially reduced afterwards, except in certain areas e.g. axilla and pudenda (Nishio, 1964). There is a radical dissimilarity between eccrine and apocrine sweat glands as regards their time of initial appearance

and mode of development (Nishio, 1964). The eccrine sweat glands developing directly from the surface epidermis are already in an advanced state of development when the primordia of apocrine glands first appear (Montagna, 1959). Nishio (1964) comments that these facts suggest that the two sweat glands have essentially different functions. The occasional apocrine duct can be found opening directly onto the skin surface, possibly because the duct aperture has been transposed from the hair follicle to the free surface (Homma, 1926). Conversely, the appertures of the eccrine ducts are never transposed to the hair follicle. Continued development of the apocrine gland primordia in regions such as the trunk, scalp and beard, after the 5th foetal month explains the presence of the so-called ectopic glands (Pinkus, 1958; Hurley and Shelley, 1960). By the 6th foetal month all the glands are elongated and coiled at the base and some of them may show the beginnings of a lumen and the more advanced glands may have a diameter larger than that of the eccrine glands. The secretory coils of both types of gland are found in the lower part of the dermis at this stage (Montagna, 1959). The apocrine glands are fully formed by the 9th foetal month. Up to this time they have been larger than the eccrine glands, but from this point their overall diameter is smaller although their lumen is larger (Montagna, 1959). In the regions where further development of the apocrine buds does not occur, the bud is eventually absorbed into the epithelium (Hurley and Shelley, 1960). Myoepithelial cells are not present in apocrine glands at birth but differentiate later (Hurley and Shelley, 1960).

Glandular anlagen are found only in a small percentage of the hair follicles in regions where the glands are not commonly found in the adult (Montagna, 1962). Montagna described the flask shaped gland anlagen as becoming elongated into solid cords, and by the 6th foetal month, the base of each cord begins to be coiled. A lumen appears first in the presumptive duct by a partial keratinization and shrivelling-up of the cells, in the centre of the coil. The clefts become more extensive and confluent in the presumptive secretory coil. The glands gradually become larger and more convoluted, attain a large lumen and resemble apocrine

sweat glands in the 7th and 8th months. Borsetto (1951) described the apocrine ducts in foetal life opening directly to the epidermal surface, but Montagna (1959) found using thick frozen sections that the majority of the ducts opened into the piliary canals, above the sebaceous glands, just as they do in the adult.

2.17.2 THE APOCRINE GLANDS FROM BIRTH TO PUBERTY AND PUBERTAL CHANGES

Undifferentiated glands are present at birth (Montagna and Parakkal, 1974). Some differentiation occurs subsequently, but development approximating to that of the adult does not occur until about 7 - 8 years of age (Montagna, 1959; Montes, Baker and Curtis, 1960). Full activation occurs during puberty in concurrence with the growth of the terminal hairs in the same regions. The ceruminous glands and the glands of Moll develop fully before birth and appear to be under a different endocrine control (Hurley and Shelley, 1960). The glands remain small but easily recognizable from the eccrine glands up to the forth postnatal year, when they begin to enlarge gradually, appearing to be differentiated and apparently functional in children of 8 years (Montagna, 1959). In adults the glands are similar to those of older children and adolescents but are larger and contain pigments, lipids and ionic iron, although the amounts of these is variable even in adults (Montagna, 1959). Montes, Baker and Curtis (1960) found some difficulty in differentiating between the two types of sweat gland in a specimen of a 4 year old child. They found the apocrine tubules to be narrow in comparison with the adult, the lining epithelium being low columnar or cuboidal with no apical pseudopodia and a poorly developed or wholly lacking brush border. Montes et al. (1960) found PAS-positive granules to be, in general, lacking at this stage, although Montagna (1959) said that they were present. Small amounts of intraluminal secretion are seen at this age (Montes et al. 1960). By the 7th or 8th postnatal year, Montes et al. (1960) noted that the cells were commonly columnar, with occasional pseudopodia and a PAS-positive brush border. PAS-positive granules and cytoplasmic RNA were all prominent. Montagna (1959) found a very thick apparently collagenous basement membrane surrounding the apocrine glands in pre-pubertal specimens, that of the eccrine

glands being much thinner. He described the apocrine glands as enlarging to such an extent by the 10th - 11th postnatal year that they begin to extend into the subcutaneous fat. Montagna (1959) described the major difference between the glands of young children and those of older children and adults as being the presence of glycogen in the former. Hurley and Shelley (1960) thought that the differentiation of the myoepithelial cells occurred postnatally and Montes et al. (1960) described them as being definitely present by 4 years of age and probably considerably before this. Borsetto (1951) found the secretory cells to be devoid of granules at birth with comparatively low cytoplasm, indicating the lack of secretory activity. Shelley and Hurley (1953) were unable to induce apocrine sweating in children.

2.17.3 THE APOCRINE GLANDS IN ADOLESCENCE AND THE YOUNG ADULT

Montagna (1959) described the apocrine glands as continuing to grow through adolescence, when the glomerate coils bulge for some distance into the subdermal fat, where they crowd against each other. In adolescent subjects, some segments of apocrine secretory tubules may be dilated and lined with an epithelium reduced to squamous cells, and other segments of the same gland may have a small lumen, lined with tall columnar cells, and this variation has been observed in the glands of young children (Montagna, 1959; Winkelmann and Hultin, 1958).

2.17.4 THE APOCRINE GLANDS IN MENSTRUATION AND PREGNANCY

It is still not clear as to whether the sexual cycles of the female have any effect upon the secretory activity of the apocrine glands. Loeschcke (1925) and Herzenberg (1927), according to Montagna and Parakkal (1974) and Montes, Baker and Curtis (1960) respectively, reported hypertrophy and hyperplasia during the premenstrual period with cytoplasmic granules and dilated tubules. Cavazzana (1947) quoted by Montagna and Parakkal (1974), and Way and Memmesheimer (1938) agreed in general with these observations.

Montagna (1956 and 1959) was unable to demonstrate any apocrine

gland changes which could be correlated with different parts of the menstrual cycle. Montagna (1959) pointed out that there was too much gland to gland variation at any one time to make any inferrence as to apocrine changes in relation to the menstrual cycle. No histochemical changes were observed. Montes et al. (1960) also found that they could not correlate any clear cytological variations with the phase of the menstrual cycle, but did claim that an increase in the number of PAS-positive granules occurred during the proliferative phase concurrently with a rising level of oestrogens. Ellis (1967) stated that there were some minor changes in the secretory cells with different reproductive states and for this reason he called the glands 'secondary sexual organs'. Montagna (1959) disagreed with the above opinion and pointed out that the apocrine glands develop before puberty and do not perish after the cessation of gonadal activity.

It is also uncertain as to whether any changes occur in the apocrine glands in relation to pregnancy. Montagna and Parakkal (1974), and Montes, Baker and Curtis (1960) state in their reviews of this subject that Talke (1903), Rebaudi (1912), Waelsch (1912), Krompecher (1919), Richter (1932) and Cavazzana (1947) all agreed that the tubules of the apocrine sweat glands were hypertrophied. Way and Memmesheimer (1938) were of the same opinion. Cavazzana (1947) and Herzenberg (1927) interpreted these changes as being indicative of increased activity. Montagna (1956 and 1959) reported that there were no structural changes which were distinctive of pregnancy. Several workers have observed that cystic tubules filled with secretion were unusually common during pregnancy. Montes et al. (1960) found some agreement with the observations of previous workers that there is some enlargement of the tubules during pregnancy. Their main observations were that early in pregnancy the intracellular PAS-positive granules were abundant and intraluminal secretion minimal, while 4½ months into the pregnancy the situation is reversed. Hurley and Shelley (1960) found no significant increase or decrease in apocrine sweat production during pregnancy or lactation. Cornbleet (1952b) considered that hidradenitis suppurativa and Fox-Fordyce disease commonly remitted or greatly improved in periods of pregnancy, but relapse

often occurred post puerperium. Cornbleet concluded that the apocrine glands were found in a resting state more often, and secrete less during pregnancy than when the subject is in the non-gravid state. Hurley and Shelley (1960) regarded this as very strong evidence for decreased apocrine activity during pregnancy.

2.17.5 AGE CHANGES IN THE APOCRINE GLANDS

Changes with age in apocrine glands are described by a number of authors (Montagna, 1956, 1959, 1974; Winkelmann and Hultin, 1958; Shelley and Cahn, 1955; Montes, Baker and Curtis, 1960). Age changes are characterised by mucoid metaplasia, cystic dilatation, atrophy and fragility of the epithelial cells (Montagna, 1959). However, with the exception of epithelial fragility, these changes may be found in the axilla at any age, even in infancy (Montagna and Parakkal, 1974). The dilatation of some segments of the apocrine gland commonly seen in old age, when parts of the gland become cystic and the character of their secretion change is called mucoid metaplasia by Winkelmann and Hultin (1958). Mucoid metaplasia begins earlier in women (around 20 years of age) than in men, but is increasingly common in men and women later in life, especially in the over-fifties (Montagna and Parakkal, 1974). Montagna (1959) describes a large number of the glands of the aged as showing the above changes, but many other glands remain intact and apparently normal. The epithelium of glands with mucoid metaplasia and cystic dilatation lose most of the normal characteristics and no longer resemble the secretory cells of normal glands. They are reduced to almost squamous in type, rarely contain pigment, lipid or iron and may show increased PAS-positivity. They have granules and plaques which stain metachromatically with toluidine blue and the contents of the tubular lumen are strongly PAS-reactive and may stain metachromatically. The staining properties are similar to those of mucus or chondroitin sulphate (Montagna, 1956). Winkelmann and Hultin (1958) pointed out that such a change is not a requisite of senescence and may not be present even in extreme old age. Similar histochemical material has been noted in the apocrine glands in Fox-Fordyce disease (Winkelmann and Montgomery, 1956; Winkelmann,

Kierland and Montgomery, 1956). Age affects apocrine sweating primarily as a result of the secretory state of the gland. In general the apocrine glands are smaller and show considerably fewer actively secreting cells with high columnar epithelium (Hurley and Shelley, 1960). Montagna (1959) found the apocrine glands to be relatively resistant to ageing. Homma (1926) did not consider it likely that the apocrine glands were reduced in old age.

2.18 RACIAL AND INTERSEXUAL VARIATIONS

Schiefferdecker (1917 - 22) was the first to note the major frequency differences of these glands among different races. He found the Australian Aboriginals to have the greatest number of apocrine glands, and the Caucasians the least. Homma (1926) found apocrine glands to be three times more common in Negroes than Caucasians. Woollard (1930) found the Australian Aboriginals to have a similar variation in the frequency of apocrine glands as Caucasians. Orientals are placed between Caucasians and Negroes as far as frequency distribution is concerned (Aoki, 1962). Hurley and Shelley (1960) described the apocrine glands of the Negroes as larger and producing greater quantities of sweat of thicker consistency.

Homma (1926) found apocrine glands to be better developed and twice as frequent in females than in males in all races. Montes, Baker and Curtis (1960) described the PAS-positive bodies as being smaller and less common in the male, with a lower secretory epithelium, and the apical cytoplasm, not as frequently raised into a high dome.

2.19 EFFECTS OF HORMONES UPON THE APOCRINE GLANDS

The natural history of the apocrine sweat glands in man suggests that they are under endocrine control. However, the precise nature of such hormonal control is not clear. Shelley and Cahn (1955b) using topical and systemic administration of oestrogens, androgens, progesterone, thyroxine, growth hormone, prolactin and chorionic gonadotrophin, alone or in various combinations,

found no appreciable alteration in apocrine sweating or in the histological appearance of the apocrine sweat glands.

Hurley and Shelley (1960) using subcutaneous implants of androgens and oestrogens, and prolactin injections, failed to detect significant variations in the quantity or quality of apocrine sweat, or in the apocrine glands themselves. They suggested that the human apocrine sweat gland may be controlled by a specific pituitary hormone, as in the case of the specific trophic factor of the anterior pituitary controlling the activity of the sebaceous gland, as described by Lorincz and Lancaster (1957).

The finding by Shelley and Butterworth (1955) of the absence of apocrine glands in mongolism, in which the pituitary, thyroid and adrenal glands show malfunction, supports the theory of hormonal control.

SECTION B

CHAPTER III

THE PATIENTS AND PATIENT CHARACTERISTICS

CONTENTS PAGE

INTRODUCTION

Patients with hidradenitis suppurativa, seen or treated by the author at the University Hospital of Wales, Cardiff, form the basis of this study. The patients were referred from various sources:- their own general practitioner, the Accident and Emergency Department, the Department of Dermatology and from other general surgeons, who were aware of the University Department of Surgery's interest in the disease.

The aim of this chapter was to document:-
the age at onset of hidradenitis; the age at presentation for surgical management; the sex and race distribution of the patients; sites involved by disease; and the nature and effect of any previous medical or surgical treatment received by the patient.

PATIENTS AND METHODS

The seventy-five patients entered into the study were interviewed by myself, and a questionnaire, Appendix 1, completed for each patient. Their age, sex, race, site/sites of involvement with hidradenitis were recorded; as was the duration of disease at each site. Note was made of any previous surgical treatment for hidradenitis at each site; including the nature of the treatment and the method used to obtain healing, with its outcome. The patients were also questioned about the nature of any previous medical therapy for the disease, and its effects.

The patients underwent a full physical examination and all sites involved by hidradenitis were noted, whether these were part of the presenting complaint or not. The diagnosis of hidradenitis rested upon its classical macroscopic appearance and the exclusion of other relevant conditions, by means of the appropriate investigations as previously described. The appearance of the diseased areas was recorded by photography.

RESULTS

3.1 AGE, SEX AND RACE

The sex distribution of the patients, their ages at the onset of hidradenitis, and their ages at presentation for definitive treatment are shown in Table 2 and Figs. 1 and 2.

Sixty of the patients were female and 15 were male, a female/male ratio of 4 : 1. The ages given at onset of hidradenitis refer to the age at which hidradenitis first occurred at any site in that patient, and the age at presentation refers to the age at which that patient first presented to the Department of Surgery for definitive management of the hidradenitis.

The age of first onset of hidradenitis ranged from 13 to 50 years for the female patients, with a mean value of 26 ± 9 and a median value of 22 years. This was little different to the age of onset in the male patients which ranged from 14 to 35 years, with a mean value of 23 ± 6 and a median value of 22 years. Both males and females were similar in that the 3rd decade produced the majority of cases; 40% of the cases arising in the 3rd decade in the males and 50% arising in the females. The 2nd and 3rd decades accounted for the majority of new cases in both sexes, the percentage of new cases in these decades being 79% for the females and 80% for the males. The sexes differed in that while no new cases of hidradenitis arose in the males after the 4th decade, the females continued to produce a small proportion of new cases into the 5th and 6th decades constituting 12% of the female numbers.

There was also little difference in the age of presentation for definitive treatment between the sexes; the age range being 16 to 59 years, with a mean value of 33 ± 10 and a median value of 32 years for the female patients, and a range of 20 to 50 years with a mean of 33 ± 8 and a median of 32 years for the males.

The duration of disease from first onset at any site, to the time of presentation for surgical ablation of the diseased area ranged from 1 - 22 years with a mean of 7 ± 6 and a median of 6 years for the females and a range of 2 - 21 years, with a mean value of

TABLE 2.

AGE AT ONSET OF HIDRADENITIS AND AT PRESENTATION FOR SURGICAL TREATMENT.

SEX	AGE AT ONSET OF HIDRADENITIS IN DECADES.					
	10 - 19	20 - 29	30 - 39	40 - 49	50 - 59	RANGE, MEAN ± SD, MEDIAN
FEMALE n = 60	16 26.7%	31 51.7%	7 11.7%	5 8.3%	2 3.3%	13 - 50 26 ± 9 22
MALE n = 15	6 40%	6 40%	3 20%	0	0	14 - 35 23 ± 6 22
SEX	AGE AT PRESENTATION FOR SURGICAL TREATMENT OF HIDRADENITIS					
	10 - 19	20 - 29	30 - 39	40 - 49	50 - 59	RANGE, MEAN ± SD, MEDIAN
FEMALE n = 60	3 5%	19 31.7%	24 40%	8 13.3%	6 10%	16 - 59 33 ± 10 32
MALE n = 15	0	4 26.7%	9 60%	1 6.65%	1 6.65%	20 - 50 33 ± 8 32

FIG. 1. AGE AT ONSET OF HIDRADENITIS SUPPURATIVA

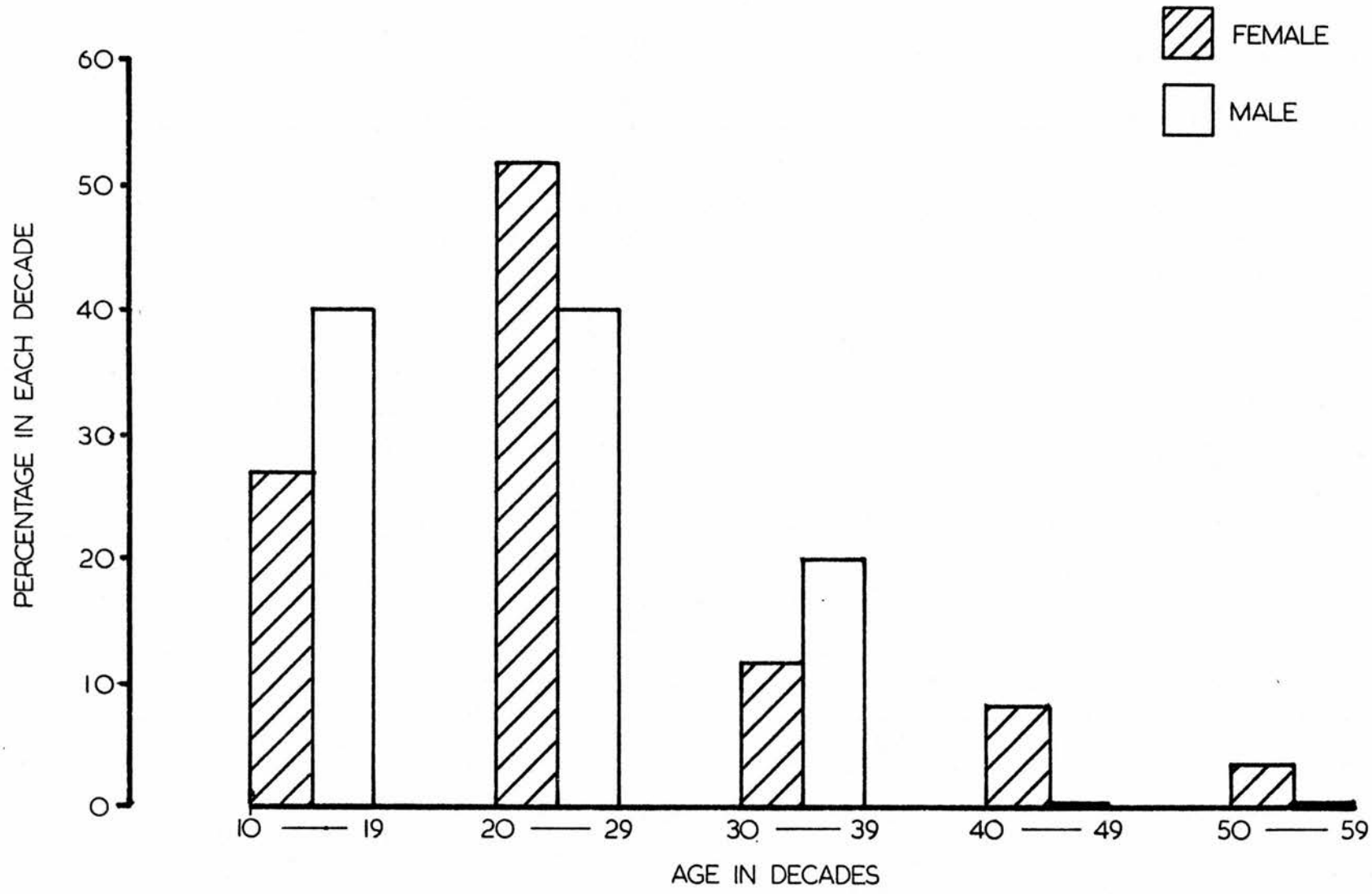
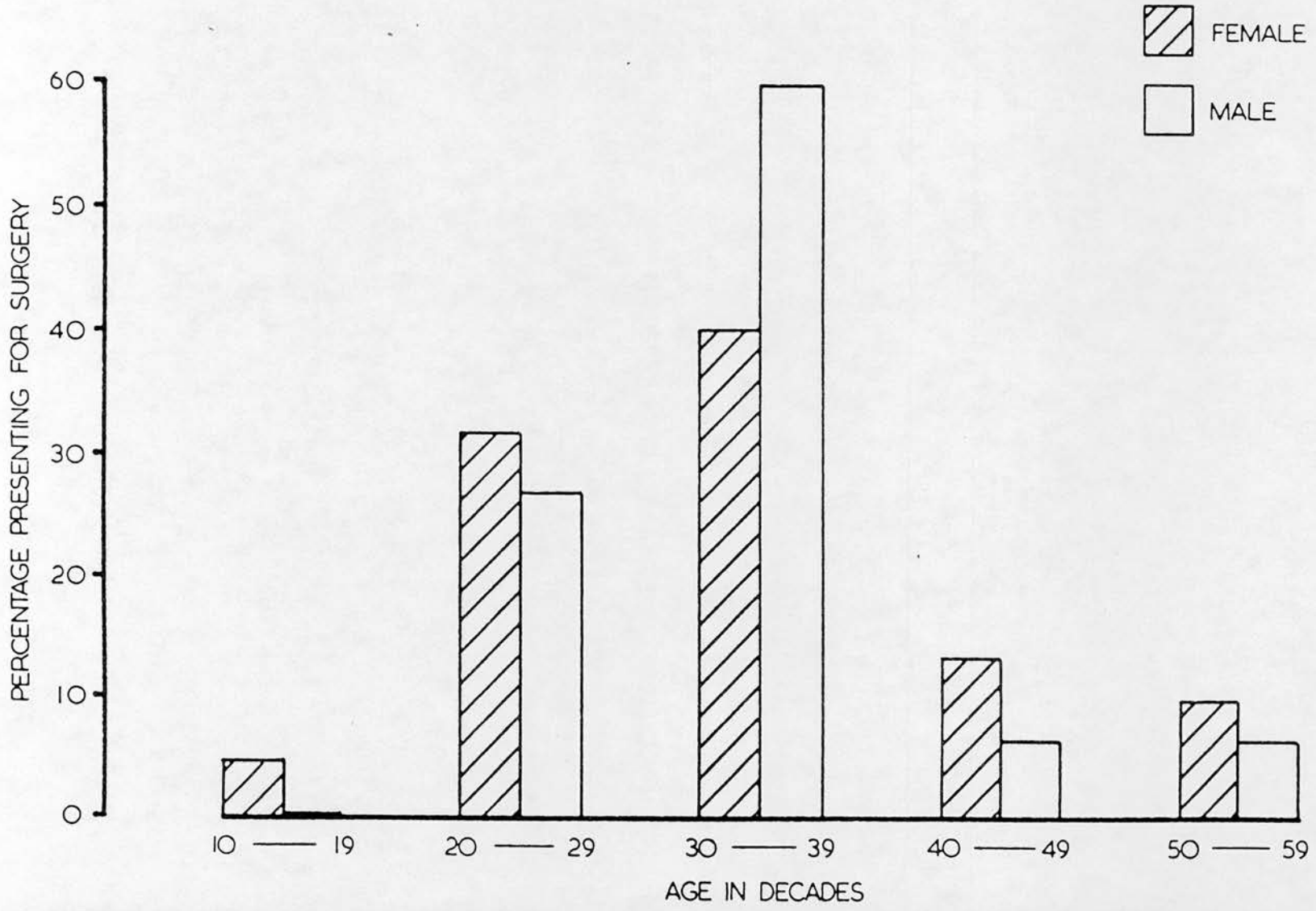


FIG. 2. AGE AT PRESENTATION FOR SURGICAL TREATMENT OF HIDRADENITIS



$10^{+}_{-}5$ and a median of 8 years for the males. Seventy-one of the patients were of European origin, and the remaining 4 of Negro, Indian, Afro-European and Indo-European origin.

3.2 SITE OF DISEASE

The sites involved by hidradenitis in the 75 patients entered in this study are shown in Fig. 3. The detailed patient data is given in Appendix 2.

The most common site of disease in the female population was the axilla, Fig. 4, 46 of the 60 female patients having axillary disease (76.6%), which was bilateral in 33 (71.7%) and unilateral in 13. Eight of the 13 cases with unilateral axillary disease had the condition confined to the right axilla and the remaining 5 cases had the disease confined to the left axilla. The next most common site for hidradenitis in the female population was the groin, Fig. 5; 27 of the 60 female patients having disease involving the groin (45%). The involvement of the groins was bilateral except in 2 cases, where the right groin only was involved. Several other sites were macroscopically involved by hidradenitis:- the labia majora 14/60 (23.3%), the pubic area 18/60 (30%), the perineum 17/60 (28.3%), the inframammary folds of the breasts 2/60 (3.3%); the perianal and the skin over the sternum were involved in 2 cases respectively. These latter sites of hidradenitis were always found in association with disease at the more major sites, e.g. the axillae or groins, except in one case each of pre-sternal, pubic and perianal disease.

Twenty-seven of the 60 female patients had axillary disease alone (45%) and 13 had disease confined to the pubo-inguino-perineal-perianal area alone (21.7%). The majority of the remainder had disease at multiple sites.

In the 15 males, the axilla was also the most common site of disease, 14 of the 15 males having axillary disease (93.3%). This was bilateral in 12 cases, the remaining 2 males having the condition in the right axilla. The next most commonly involved site in

FIG. 3. SITES INVOLVED BY HIDRADENITIS

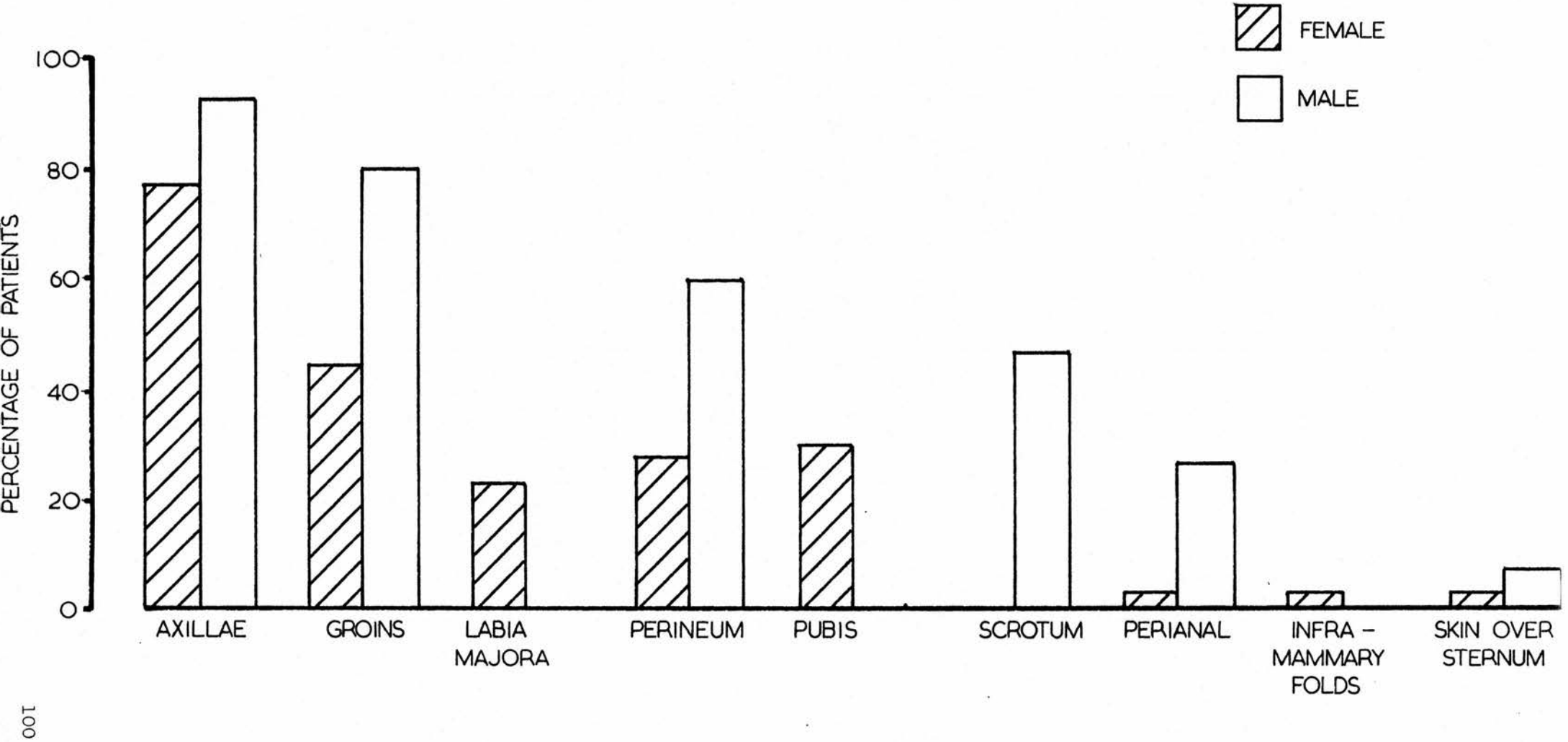


FIG. 4. HIDRADENITIS SUPPURATIVA IN THE AXILLA.

FIG. 5. HIDRADENITIS SUPPURATIVA IN THE FEMALE PUBO-INGUINO-PERINEAL AREA.

the males was the groin, 12 of the 15 males having disease in this area (80%), a higher proportion than in the female subjects. The groin hidradenitis was bilateral in 11 of the 12 males (91.7%), Fig. 6. Other sites involved in the 15 males included the perineum, 9 cases (60%); the scrotum 7 cases (46.7%); the perianal area 4 cases (26.7%); and the pre-sternal skin and the nape of the neck in one case each. Hidradenitis in these latter areas was always associated with disease in the axillae or groins. The axillae alone were involved in 3 cases (20%) and the pubo-inguino-perineal area plus adjacent skin alone in one case. The males had a much higher incidence of disease at multiple sites than was found in the female population, Fig. 7.

In the case of the patients with bilateral axillary disease (45 patients), 31 patients (68.9%) had developed involvement of both axillae synchronously (within a few weeks of one another). In the remaining 14 patients, with initially unilateral axillary involvement, hidradenitis had developed in the contralateral axilla after an interval ranging from 6 months to 8 years, with a median interval of 15 months (mean 2.17 $\pm$ 1.96 years).

Eighteen of the 60 female patients had both axillary and pubo-inguino-perineal disease which had appeared synchronously in both regions in 6 patients (33%). In 8 patients, hidradenitis commenced in the axillae and appeared in the pubo-inguino-perineal after intervals ranging from one to 17 years, with a median interval of 3.5 years (mean 4.3 $\pm$ 4.7 years). In the remaining 4 patients, hidradenitis first occurred in the pubo-inguino-perineal region and later appeared in the axillae, at intervals ranging from one to 5 years, with a median value of 2 years (mean 2.6 $\pm$ 1.6 years).

Eleven of the male patients had disease in both the axillae and pubo-inguino-perineal areas. In 2 of these patients hidradenitis had developed synchronously in both areas. Seven patients had developed hidradenitis in the axillae initially, with its later appearance in the pubo-inguino-perineal area, at an interval ranging from one to 11 years (median 4, mean 4.7 $\pm$ 3.1 years). Hidradenitis

FIG. 6. HIDRADENITIS SUPPURATIVA IN THE MALE PUBO-INGUINO-PERINEAL AREA.

FIG. 7. HIDRADENITIS SUPPURATIVA IN THE PERIANAL AREA.

had commenced in the pubo-inguino-perineal area in the remaining 2 patients, and had later appeared in the axilla after 4 and 12 respectively.

3.3 TREATMENT RECEIVED PRIOR TO ENTRY INTO THE STUDY

All 75 patients entering the study had received one or more courses of antibiotics from their family practitioners, during acute exacerbations of hidradenitis. Few patients were aware of the names of the antibiotics they had received, but Ampicillin, Cloxacillin, Penicillin, various Cephalosporins and Septrin were mentioned.

Sixty-three of the 75 patients stated that the antibiotics they had received had failed to influence the severity of the disease.

Twelve patients stated that the antibiotics had helped in limiting the duration of exacerbations, often by bringing abscesses to a head. However, in no case had the use of antibiotics prevented further recurrence of hidradenitis.

Thirteen of the 75 patients had also bathed the diseased skin with solutions of Hibitane, Phisohex or Betadine. These antiseptic preparations had not resulted in any noticeably beneficial effect.

Thirty of the 75 patients had undergone multiple incision and drainage procedures of the abscesses/inflammatory nodules, associated with hidradenitis in the axillae and pubo-inguino-perineal areas. Many of these procedures had been performed by the patients' general practitioners in their surgeries in addition to those performed in hospital casualty departments. Frank pus was not always obtained on incising these lesions. The number of incision and drainage procedures undergone by the patients with a long history of hidradenitis or who had undergone many such procedures must be regarded as only approximate figures, as many patients found accurate recall difficult in these circumstances.

Twenty-two of the 30 patients underwent incision and drainage of axillary abscesses.

The frequency of such procedures ranged from one such procedure over a period of 20 years to 6 such procedures in the course of one year. The median number of such procedures in the axilla was 0.85/patient/year (mean 1.44 $\pm$ 1.7/patient/year). However, 4 of the 22 patients underwent 4 or more drainage procedures within one year. The periodicity of axillary drainage procedures ranged from 2 months to 20 years, with a median interval between such procedures of 1.2 years (mean 3.72 $\pm$ 5.69 years).

Thirteen patients underwent incision and drainage of lesions in the pubo-inguino-perineal region. The frequency of these procedures ranged from one drainage procedure in 20 years to 12 such operations during a period of 8 years, with a median value of 0.6 procedures/patient/year (mean 0.73 $\pm$ 0.53 procedures/patient/year). The periodicity of drainage procedures in this region ranged from 8 months to 20 years, with a median interval between such procedures of 1.8 years (mean 4.67 $\pm$ 6.14 years).

It was the general experience of the patients concerned, that incision and drainage resulted in abatement of that particular exacerbation, but had no influence on the recurrent and chronic course of the disease.

Two patients had undergone axillary excisions confined to removal of visibly diseased skin (there had been no attempt at complete excision of the apocrine gland containing skin in the diseased area), before entering this study. Four patients had previously undergone excisions of a similar extent in the groins; recurrent disease had developed in all cases. One patient presenting to this study with pubo-inguino-perineal disease, had previously received a radical bilateral axillary skin excision for hidradenitis at another centre. The axillary defects had been covered with split skin grafts, and there was no evidence of recurrent disease at the time of entry to this study.

DISCUSSION

3.1 AGE, SEX AND RACE

The review of the literature suggests that the maximum incidence of hidradenitis occurs in the 2nd and 3rd decades of life, with most cases presenting for treatment in the 2nd, 3rd and 4th decades. In our series, the age at onset of hidradenitis ranged from 13 to 50 years, with a median value of 22 years for the females; and 14 to 35 years with a median value of 22 years for the males. Both sexes were similar in that the second and third decades of life produced the majority of new cases. The median at at presentation for definitive treatment in our study was 32 years for both females and males. Our findings are thus similar to those of other reported series.

Ching and Stahlgren (1965) reported a significant incidence of new disease in the 4th, 5th and 6th decades. A similar result was obtained regarding the female patients in this study; 12% of new cases arising during the 5th and 6th decades. However, no new cases were seen after the 4th decade in the males entering this study. Unlike Tachau (1939) and Ajayi and Olurin (1970) we did not see any cases of hidradenitis occurring in pre-pubertal children.

Ching and Stahlgren (1965), Jackman and McQuarrie (1949) and Tasche et al. (1975) all reported a predominance of Negro subjects in their series. Mustafa et al. (1980) and O'Brien et al. (1976) stated that hidradenitis was more common in Negroes. None of the above authors related the proportion of Negroes presenting with hidradenitis, to the proportion of Negroes in the catchment area of their medical practice. In our own series, 71 of the 75 patients were of European origin, the remaining 4 patients were of Negro, Indian, Afro-European and Indo-European origin. The distribution of races, or racial mixes in our catchment area is unknown. However, a marked European predominance exists which is sufficient to explain our figures. It is possible that papers reporting a Negro predominance amongst hidradenitis patients have a Negro predominance in the population of their catchment area.

Nance (1970) pointed out that overall, women were affected with hidradenitis three times more commonly than men. Similarly, there was a female predominance in our series of 4 : 1. The reason for this marked female predominance remains unclear, but an endocrine influence presumably exists, as hidradenitis is uncommon before the menarche and is once more uncommon in the post-menopausal years.

3.2 SITES INVOLVED BY HIDRADENITIS

The most common site of involvement with hidradenitis in both the females and males in this study was the axilla; 77% and 93% of the females and males respectively having axillary disease. The disease was bilateral in 72% of the female patients and in 86% of the male patients. The proportion of patients in our study having bilateral axillary involvement is similar to that of Bell and Ellis (1978) but differs markedly from that of Tachau (1939), who reported a figure of 26%.

In both the males and females the next most commonly involved site was the groins; 80% of the males and 45% of the females. In the females, there was an appreciable degree of involvement of the pubic and perineal areas and the labia majora. In the male, the perineal, perianal, scrotal and sacral areas were similarly involved. Involvement of other sites by hidradenitis was relatively uncommon. There was a trend towards disease at multiple sites in the males as compared to the females; 27% of the males as compared to 65% of the females having disease confined to either the axillae or pubo-inguino-perineal area only.

The majority of patients with bilateral axillary disease developed such involvement synchronously, but metachronous involvement of the contralateral axilla occurred after widely varying intervals. Again synchronous involvement of the axillae and pubo-inguino-perineal regions occurred, but metachronous involvement of these regions was not uncommon. This suggests that local factors are probably important in the triggering of hidradenitis at a particular site, while not excluding a systemic predisposition to the disease.

3.3 PREVIOUS MEDICAL AND SURGICAL TREATMENT

Our patients' experience of previous treatment received before entering this study was noted; but it is not necessarily representative of hidradenitis patients as a whole. This is because the majority of our patients had active, chronic, progressive disease and were, therefore, a selected population in which the previous management had failed.

Mustafa (1980) considered antibiotics to be of use in the acute stage, when continued for an adequate duration and based upon culture and sensitivity studies. However, he did not produce any data to support this belief. The only reported controlled trial of the use of antibiotics in hidradenitis has been produced by Clemmensen (1983). He reported 30 patients with recurrent hidradenitis, entered into a double blind trial to evaluate the effect of topical Clindamycin against placebo in the disease. Twenty-seven patients completed the three months treatment. The overall effect of Clindamycin treatment based on the patients' assessment of the number of abscesses, inflammatory nodules and pustules was significantly better than placebo at each monthly evaluation ($P < 0.01$). However, when each parameter was evaluated separately, Clindamycin was only significantly superior to placebo, in the reduction of the number of pustules experienced.

The majority of our patients had been treated with various antibiotics on several occasions, prior to their referral to our department, often without the benefit of culture and sensitivity testing. The duration of such treatment is unknown, depending upon the dose prescribed and the patients' compliance in completing the course of treatment. While accepting that this information is inadequate, it is of interest that few of our patients considered that the antibiotics had helped them.

Further controlled trials of antibiotic therapy in early hidradenitis, based upon culture and sensitivity testing are necessary, and should take into consideration the reports by Smith and Ropes (1945), Biegelman and Rantz (1949, Leach et al. (1979) and Brenner and

Lookingbill (1980) of the isolation of bacteroides from the lesions of hidradenitis.

Incision and drainage brought local relief, where pointing abscesses were present, but had no influence upon the recurrent and progressive course of the disease.

Local excisions had a high recurrence rate and should be probably regarded as a temporising measure while awaiting the full extent of the disease to make itself obvious. In the one case referred, where a radical excision of hidradenitis at another site had been previously performed, it had been successful.

CHAPTER IV

AETIOLOGICAL AND ASSOCIATED FACTORS

CONTENTS PAGE

CONTENTS PAGE

CONTENTS PAGE

INTRODUCTION

The aetiology of hidradenitis suppurativa remains unclear. With a view to determining some of the mechanisms involved in the production of hidradenitis, the following factors were chosen for examination, for the reasons given below.

4.1 HIDRADENITIS AND IRON DEFICIENCY ANAEMIA

Tennant et al. (1968) reported an association between hidradenitis and iron deficiency anaemia. The haemoglobin values of the patients entering the study were, therefore, noted so as to determine whether this was a primary association or secondary to complications of the disease.

4.2 PREVALENCE OF DIABETES MELLITUS IN HIDRADENITIS PATIENTS AND THEIR FAMILIES

Chronic infections are more common in patients with diabetes mellitus. Chapman (1972) found diabetes in 10% of his series of patients, and Bell and Ellis (1978) found a positive family history of diabetes in 12.5% of their patients. The question as to whether an association between hidradenitis and diabetes exists is, therefore, relevant. The hidradenitis patients were screened for the presence of diabetes, either by fasting venous plasma glucose levels or by the performance of a glucose tolerance test. Their family history for diabetes was compared with that of a normal control population.

4.3 A COMPARISON OF THE ABO AND RHESUS BLOOD GROUPS IN HIDRADENITIS PATIENTS, AS COMPARED TO THE PROPORTION OF THOSE GROUPS IN THE NORMAL POPULATION

Both the ABO and Rhesus red cell antigens are inherited from one's parents; the ABO antigens as simple mendelian characters and the Rhesus antigens by a more complex process.

The importance of the ABO antigens as inherited characteristics, is demonstrated by the fact that when tissues are transplanted,

graft rejection is hastened by donor-recipient ABO incompatibility. Furthermore, significant departures from ABO frequencies have been observed in patients with various kinds of disorders. Group A individuals have been reported to be more susceptible to gall stones, cirrhosis of the liver, and tumours of the salivary glands, stomach and pancreas. (Wintrobe 1974)

The ABO and Rhesus blood groups of the hidradenitis patients were, therefore, examined to see if there was any association between hidradenitis and a particular blood group, as some evidence of a genetic transmission of disease susceptibility.

4.4 FAMILY HISTORY OF HIDRADENITIS SUPPURATIVA IN HIDRADENITIS PATIENTS AS COMPARED TO NORMAL CONTROLS

Little attention has been paid in past literature to the family history of hidradenitis patients. A significant increase in a positive family history of hidradenitis in hidradenitis patients when compared with a normal control population would suggest either a genetic transmission of disease susceptibility or alternatively a common exposure to an environmental agent by that family. For this reason, the family history of hidradenitis patients and controls were compared for the prevalence of hidradenitis.

4.5 THE PREVALENCE OF ACNE VULGARIS, SEBACEOUS (EPIDERMOID) CYSTS, IN HIDRADENITIS PATIENTS AS COMPARED TO A NORMAL POPULATION

The condition most commonly reported to be associated with hidradenitis is acne vulgaris. Steiner and Greyson (1955) and Conway, Stark and Climo (1952) reported that 75% and 70% of their hidradenitis patients respectively, had active acne or evidence of severe past acne. Anderson and Dockerty (1958), however, found acne to be present in only 30% of their patients with perianal hidradenitis. Knaysi et al. (1968) found an increased incidence of sebaceous (epidermoid) cysts, 9% in their series of hidradenitis patients. Brunsting (1952) described an association between chronic hidradenitis, dissecting cellulitis of the scalp, and acne conglobata involving

the face, neck and back. The basic lesion in all three conditions being follicular occlusion caused by hyperkeratotic plugging.

An increased prevalence of acne vulgaris and sebaceous cysts in hidradenitis patients as compared to normal controls, would be supporting evidence that hyperkeratotic follicular occlusion is an important mechanism in the aetiology of hidradenitis.

4.6 THE PREVALENCE OF HYPERSENSITIVITY REACTIONS IN HIDRADENITIS PATIENTS AS COMPARED TO NORMAL CONTROLS

Bell and Ellis (1978), found an abnormally high incidence of atopic reactions in their series of hidradenitis patients; this related in particular, to hay fever, penicillin and Elastoplast. The major allergen in the Elastoplast adhesive being colophony. Bell and Ellis (1978) communicated personally with Smith and Nephew Ltd., who ascertained the expected incidence of allergy to colophony to be around 2%.

An unexpectedly high incidence of atopy in hidradenitis patients as compared to a normal population, would raise the possibility that the initial change in hidradenitis may be a hypersensitivity reaction to some environmental agent.

4.7 THE USE OF DEPILATION, DEODORANTS AND TALCUM POWDER IN HIDRADENITIS PATIENTS PRIOR TO THE ONSET OF THE DISEASE AS COMPARED TO NORMAL CONTROLS

The hypothesis that mechanical shaving and the use of agents such as chemical depilatories and deodorants are implicated in the aetiology of hidradenitis, has often been implied, but has never been tested. The purpose of this section of the study, was to ascertain as to whether hidradenitis patients, had made more frequent use of the above agents, prior to the onset of the disease, than a normal control population.

4.8 THE INFLUENCE OF MENSTRUAL PERIODS AND PREGNANCY UPON HIDRADENITIS

The appearance of hidradenitis after puberty; its maximum incidence during the reproductive years and the decline of the disease during the climacteric, suggests that there is an endocrine influence upon the activity of the disease. However, the nature and mechanisms of this influence is not understood. It might be expected that the fluctuations in hormone levels that accompany the menstrual cycle and pregnancy may have an effect upon the activity of hidradenitis, which may in turn provide assistance in understanding the mechanism involved. It was the purpose of this section to detail the changes experienced by female hidradenitis patients during their menstrual cycle and pregnancies.

PATIENTS AND METHODS

4.1 HIDRADENITIS AND IRON DEFICIENCY ANAEMIA

Seventy-five patients (60 female and 15 male) with hidradenitis had their haemoglobin levels determined by the Coulter Senior Automated Analysis System, at the time of their admission to the study.

4.2 PREVALENCE OF DIABETES MELLITUS IN HIDRADENITIS PATIENTS AND THEIR FAMILIES

Eighty-three hidradenitis patients were screened for the presence of diabetes mellitus. None of the patients were known diabetics or had symptoms of diabetes. Twenty-seven of the patients underwent a glucose tolerance test and fifty-six patients had a fasting venous plasma glucose level performed, as defined by the WHO Expert Committee on Diabetes Mellitus (2nd report).

Fifty-eight patients (45 female and 13 male) with hidradenitis were questioned about a family history of diabetes, amongst their first and second degree relatives. A family tree was constructed for each patient and completed for the presence or absence of diabetes amongst those relatives.

One hundred and twenty-four patients (81 female and 43 male) attending the outpatients department of the University Hospital of Wales were interviewed as normal controls. They were collected on a 2:1 female:male ratio, and age matched to within two years of the ages of the hidradenitis patients. They were acquired on a completely random sequential basis, which depended solely upon the date of their referral to the outpatients department. The only patients excluded from this study were patients with hidradenitis or other chronic skin conditions, and ano-rectal inflammatory bowel disease. The predominant reasons for referral among the control patients were breast pathology, gall bladder disease, herniae and varicose veins. Again, a family tree was constructed and the presence of diabetes among relatives sought.

4.3 A COMPARISON OF THE ABO AND RHESUS BLOOD GROUPS IN HIDRADENITIS PATIENTS, AS COMPARED TO THE PROPORTION OF THOSE GROUPS IN THE NORMAL POPULATION

The A, B, AB, O and Rhesus blood groups were determined by standard laboratory methods (Dacie and Lewis) for the initial forty-four hidradenitis patients admitted to this study. The relative proportions of these groups in the hidradenitis patients, were then compared with the proportion of those groups in the South Wales Blood Transfusion Service donor panel patients, as the group most likely to represent the normal population.

4.4 FAMILY HISTORY OF HIDRADENITIS SUPPURATIVA IN HIDRADENITIS PATIENTS AS COMPARED TO NORMAL CONTROLS

Fifty-eight hidradenitis patients (45 female and 13 male) were questioned about the prevalence of hidradenitis in first and second degree relatives, and a family tree drawn up for each patient. The same group of normal control patients as used in section 2 were also interviewed in order to determine their family history of hidradenitis. It was possible to interview and examine all of the relatives who were claimed to suffer from hidradenitis and to confirm the diagnosis.

4.5 THE PREVALENCE OF ACNE VULGARIS, SEBACEOUS (EPIDERMOID) CYSTS, IN HIDRADENITIS PATIENTS AS COMPARED TO A NORMAL POPULATION

The prevalence of acne vulgaris and sebaceous (epidermoid) cysts were determined from the recordings made on the protocol sheets of fifty-eight hidradenitis patients (13 male and 45 female). A 'normal' control population of forty-two males and eighty females were gathered from patients attending outpatients at the University Hospital of Wales by a similar method and with the same exclusions as previously described in section 2. These patients were interviewed with regard to their present or past history of acne vulgaris and sebaceous cysts.

4.6 THE PREVALENCE OF HYPERSENSITIVITY REACTIONS IN HIDRADENITIS PATIENTS AS COMPARED TO NORMAL CONTROLS

The prevalence of drug allergy, hay fever, asthma, allergy to Elastoplast, or history of other allergic manifestation was obtained from the protocol sheets for fifty-eight hidradenitis patients (13 male and 45 female). The prevalence of the above factors in the one hundred and twenty-two control patients previously described in section 5 was then compared with the results obtained for the hidradenitis patients.

4.7 THE USE OF DEPILATION, DEODORANTS AND TALCUM POWDER IN HIDRADENITIS PATIENTS, PRIOR TO THE ONSET OF THE DISEASE, AS COMPARED TO NORMAL CONTROLS

Forty hidradenitis patients (32 female and 8 male), were questioned about the use of the above agents, in the axillae and pubo-inguino-perineal regions, prior to the onset of hidradenitis. Positive use of an agent was recorded when the patient had made daily use of that agent in their personal hygiene routine for a minimum period of six months.

Of the thirty-two female patients, twenty-four had axillary disease (75%), twenty-three had inguinal disease (71%) and fifteen had both (46.9%). All the male patients had axillary disease and seven had inguinal disease, in addition (87.5%). The ages of these patients at the onset of hidradenitis ranged from 15 - 49 years of age.

The same one hundred and twenty-two age and sex matched control patients as used in section 5 were also questioned about the use of the above agents. Because of patient variation in the brands of preparations used, the patients were questioned about the use of chemical depilatories, deodorants and anti-perspirants, as broad categories.

4.8 THE INFLUENCE OF MENSTRUAL PERIODS AND PREGNANCY UPON HIDRADENITIS

Forty-five women with hidradenitis were questioned about the activity of their disease in relation to menstrual periods and pregnancy.

RESULTS

4.1 HIDRADENITIS AND IRON DEFICIENCY ANAEMIA

The haemoglobin values in the sixty female patients entering the study, ranged from 12.6 to 15.4 g/dl. The mean value being 13.9 g/dl. In the case of the fifteen males in the study, the haemoglobin values ranged from 14.2 to 17.2 g/dl. with a mean value of 15.6 g/dl. Four of the fifteen males had haemoglobin values of greater than 16 g/dl., exceeding the upper limit of normal for the Cardiff area. There was no case of iron deficiency anaemia.

4.2 PREVALENCE OF DIABETES MELLITUS IN HIDRADENITIS PATIENTS AND THEIR FAMILIES

None of the fifty-six patients who were screened by means of a fasting venous plasma glucose had levels above 6.0 mmol./l. and all had negative urinanalysis, thus excluding diabetes mellitus (WHO Expert Committee 2nd Report).

The results of the twenty-seven patients who underwent a glucose tolerance test are shown in Appendix 3.

The WHO Expert Committee on Diabetes Mellitus defined a two hour venous plasma value of 11 mmol./l. or greater after a 75g. glucose load, as being diagnostic of diabetes, with one additional abnormal glucose value being needed to confirm the diagnosis, in the absence of symptoms e.g. a one hour post glucose value of 11 mmol./l. or more during the first test or an elevated two hour or fasting glucose value, on a subsequent occasion. Two hour post glucose values, in the range 8 - 11 mmol./l., were termed 'impaired glucose tolerance'.

Of the twenty-seven patients having a glucose tolerance test one patient had impaired glucose tolerance, as defined by WHO criteria, with a two hour post glucose value of 10.3 mmol./l. This patient also had raised 30, 60 and 90 minute post glucose values, with a positive urinanalysis at one and two hours, and may well become frankly diabetic in later years.

Two of the thirteen male hidradenitis patients (15%) and sixteen

of the forty-five female hidradenitis patients (36%) gave a family history of diabetes mellitus, as compared to twelve (28%) of the forty-three male controls and twenty-seven (33%) of the eighty-one female controls. These differences did not reach statistical significance (x^2 test).

4.3 A COMPARISON OF THE ABO AND RHESUS BLOOD GROUPS IN HIDRADENITIS PATIENTS, AS COMPARED TO THE PROPORTION TO THOSE GROUPS IN THE NORMAL POPULATION

The results are shown in Table 3. The potential differences exist in the A and O groups. Blood group A being present in 52% of the hidradenitis patients and in 42% of the controls; blood group O being present in 34% of the hidradenitis patients and in 47% of the controls.

The ABO comparison between hidradenitis cases and controls is not significant ($x^2_3 = 3.0$), $p > 0.1$.

The Rhesus comparison also shows no significant difference ($x^2_1 = 0.128$), $p > 0.1$.

4.4 FAMILY HISTORY OF HIDRADENITIS SUPPURATIVA IN HIDRADENITIS PATIENTS AS COMPARED TO NORMAL CONTROLS

Five of the thirteen male hidradenitis patients (38%) and eleven of the forty-five female hidradenitis patients (24%), had a positive family history of hidradenitis as compared to none of the forty-three male controls and to one of the eighty-one female controls. The increased family history of hidradenitis, amongst male, female and hidradenitis patients as a whole was significant when examined using the x^2 test with p values of 0.001, 0.00001, and 0.000001 respectively.

4.5 THE PREVALENCE OF ACNE VULGARIS, SEBACEOUS (EPIDERMOID) CYSTS, IN HIDRADENITIS PATIENTS AS COMPARED TO A NORMAL POPULATION

The results are shown in Table 4. Seven of the thirteen male

TABLE 3.

BLOOD GROUPS IN HIDRADENITIS PATIENTS AND SOUTH WALES BLOOD TRANSFUSION SERVICE PANEL PATIENTS.

BLOOD GROUPS	HIDRADENITIS PATIENTS		PANEL PATIENTS
A	23/44	52%	42%
B	4/44	9%	9%
O	15/44	34%	47%
AB	2/44	5%	3%
RHESUS POSITIVE	36/44	82%	85%
NEGATIVE	8/44	18%	15%

x^2 test.

ABO (Hidradenitis - Controls) $x_3^2 = 3.0$ $p > 0.1$.

Rhesus (Hidradenitis - Controls) $x_1^2 = 0.128$ $p > 0.1$.

TABLE 4. THE PREVALENCE OF ACNE VULGARIS AND SEBACEOUS CYSTS IN HIDRADENITIS (H.S.) PATIENTS AS COMPARED TO CONTROLS.

	MALE H.S. n = 13	FEMALE H.S. n = 45	H.S.(BOTH SEXES) n = 58	MALE CONTROLS n = 42	FEMALE CONTROLS n = 81
ACNE VULGARIS	7(54%) p<0.002	12(27%) p<0.05	19(33%) p<0.001	5(12%)	9(11%)
SEBACEOUS CYSTS	5(39%) p<0.05	7(16%) n.s.	12(21%) p<0.01	4(10%)	5(6%)

WITHIN SEXES BY x^2 WITH YATES CORRECTION.

BOTH SEXES ANALYSIS BY MARTAEL-HAENSEL TEST WITH CONTINUITY CORRECTION.

hidradenitis patients suffered from acne vulgaris (54%) as compared to five of the forty-two male controls (12%). Twelve of the forty-five female hidradenitis patients (27%) suffered from acne as compared to nine of the eighty-one female controls (11%). The prevalence of acne vulgaris was increased in both the male and female hidradenitis patients as compared to normal controls. When these differences were examined using the x^2 test, there were significant increases in the prevalence of acne for male hidradenitis, female hidradenitis and hidradenitis patients as a whole, with p values of 0.002, 0.05 and 0.001 respectively.

Five of the thirteen male hidradenitis patients (39%) and seven of the forty-five female hidradenitis patients (16%) had sebaceous (epidermoid) cysts as compared to four of the forty-two male controls (10%) and five of the eighty female controls (6%). When these differences were examined using the x^2 test, there were significant increases in the prevalence of sebaceous cysts amongst the male hidradenitis patients and hidradenitis patients as a whole, when compared to normal controls with p values of 0.05 and 0.01 respectively. The increased prevalence of sebaceous cysts in the female hidradenitis patients was not significant (x^2 test).

4.6 THE PREVALENCE OF HYPERSENSITIVITY REACTIONS IN HIDRADENITIS PATIENTS AS COMPARED TO NORMAL CONTROLS

The results are shown in Table 5. When the prevalence of allergic responses to drugs, in particular, antibiotics, hay fever, asthma, allergy to other materials, in hidradenitis patients was compared with the normal controls, there were no significant differences in the prevalence of these factors between the two groups, even if each sex was analysed separately.

However, a difference between the sexes emerged in relation to allergic reaction to Elastoplast specifically. Four of the thirteen male hidradenitis patients gave a history of allergy to Elastoplast (31%), as compared to two of the forty-two male controls (5%). Nine of the forty-five female hidradenitis patients (20%) gave a history of allergy to Elastoplast, as compared to a prevalence

TABLE 5	THE PREVALENCE OF ALLERGIES IN HIDRADENITIS (H.S.) PATIENTS AS COMPARED TO CONTROLS.				
	MALE H.S. n = 13	FEMALE H.S. n = 45	n = 58. H.S. BOTH SEXES.	MALE CONTROLS n = 42	n = 80 FEMALE CONTROLS
DRUG ALLERGY	1(8%) n.s.	5(11%) n.s.	6(10%) n.s	4(10%)	11(14%)
HAY FEVER	1(8%) n.s.	7(16%) n.s.	8(14%) n.s.	7(17%)	14(18%)
ASTHMA	1(8%) n.s.	3(7%) n.s.	4(7%) n.s.	4(10%)	6(8%)
ELASTOPLAST	4(31%) $p<0.05$.	9(20%) n.s.	13(22%) n.s.	2(5%)	12(15%)
ALLERGY	5(39%) n.s.	21(47%) n.s.	26(45%) n.s.	17(40%)	47(58%)

WITHIN SEX ANALYSIS BY 2 TAILED FISHER-EXACT TEST.

BOTH SEXES ANALYSIS BY MANTEL-HAENSSEL TEST.

in the female control groups of 12/80 or 15%. The increased prevalence of Elastoplast allergy in the male hidradenitis patients, when examined using the 2-tailed Fisher exact test showed a p value of 0.05, implying a significant difference. However, the increased prevalence of Elastoplast allergy in the female hidradenitis patients, was not significant when examined by the same method. When the sexes were combined, and the controls and hidradenitis patients compared for Elastoplast allergy, using the Mantel-Haenssel test with continuity correction, there was no significant difference in the prevalence of Elastoplast allergy between the two groups.

4.7 THE USE OF DEPILATION, DEODORANTS AND TALCUM POWDER IN HIDRADENITIS PATIENTS, PRIOR TO THE ONSET OF THE DISEASE, AS COMPARED TO NORMAL CONTROLS

The results are shown in Table 6, Figs. 8 and 9. In the twenty-four female patients with axillary hidradenitis, 87.5% of the patients made use of mechanical shaving, and 29.2% used chemical depilatories, as compared to 75% and 23.8% of the controls respectively. The same patients showed a reduced use of deodorants in the axilla (75%) as compared to normal controls (88.8%). The use of mechanical shaving (0), chemical depilatories (0), and deodorants (0) in the pubo-inguino-perineal area was reduced in the twenty-three hidradenitis patients as compared to the eighty controls; 16.3%, 2.5% and 3.8% respectively.

In the eight male hidradenitis patients with axillary disease, 62.5% made use of deodorants, as compared to 50% of the forty-two normal controls. None of the male hidradenitis patients had mechanically shaved the axilla as compared to 7% of the forty-two controls. Chemical depilatories had not been used in the axilla, by either male hidradenitis patients or controls.

None of the seven male hidradenitis patients made use of mechanical shaving, chemical depilatories and deodorants in the pubo-inguino-perineal area, as compared to 2.4%, 0, and 7.1% respectively of the forty-two male controls.

TABLE 6. USE OF DEPILATION, DEODORANTS AND TALCUM POWDER IN PRE-ONSET HIDRADENITIS PATIENTS AND CONTROLS.

GROUP	FEMALES							
	AXILLA				PUBO-INGUINO-PERINEUM			
	HIDRADENITIS n = 24		CONTROLS n = 80		HIDRADENITIS n = 23		CONTROLS n = 80	
	Shaving	Depilatories	Deodorants	Talcum Powder	Shaving	Depilatories	Deodorants	Talcum Powder
Hidradenitis	21 (87.5%)	7 (29.2%)	18 (75%)	9 (37.5%)	0	0	0	5 (21.7%)
	n.s.	n.s.	n.s.	$x^2 = 4.63 p < 0.05$	n.s.	n.s.	n.s.	$x^2 = 7.19 p < .01$
Controls	60 (75%)	19 (23.8%)	71 (88.8%)	52 (65%)	13 (16.3%)	2 (2.5%)	3 (3.8%)	45 (56.3%)
GROUP	MALES							
	AXILLA				PUBO-INGUINO-PERINEUM			
	HIDRADENITIS n = 8		CONTROLS n = 42		HIDRADENITIS n = 7		CONTROLS n = 42	
Hidradenitis	0	0	5 (62.5%)	2 (25%)	0	0	0	1 (14.3%)
	n.s	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Controls	3 (7%)	0	21 (50%)	16 (38%)	1 (2.4%)	0	3 (7.1%)	17 (40.5%)

X^2 TEST

FIG. 8. HYGIENE IN THE AXILLA

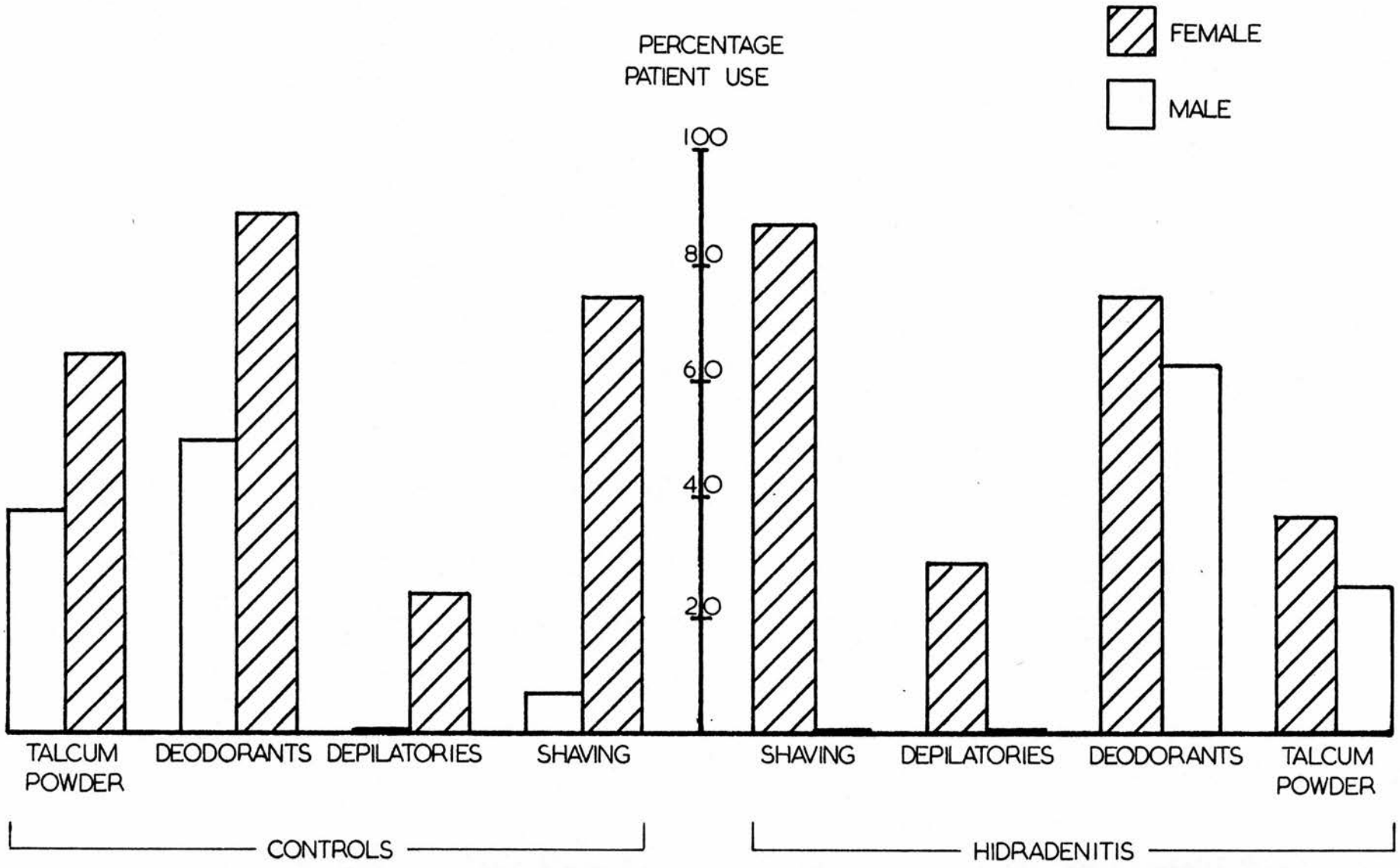
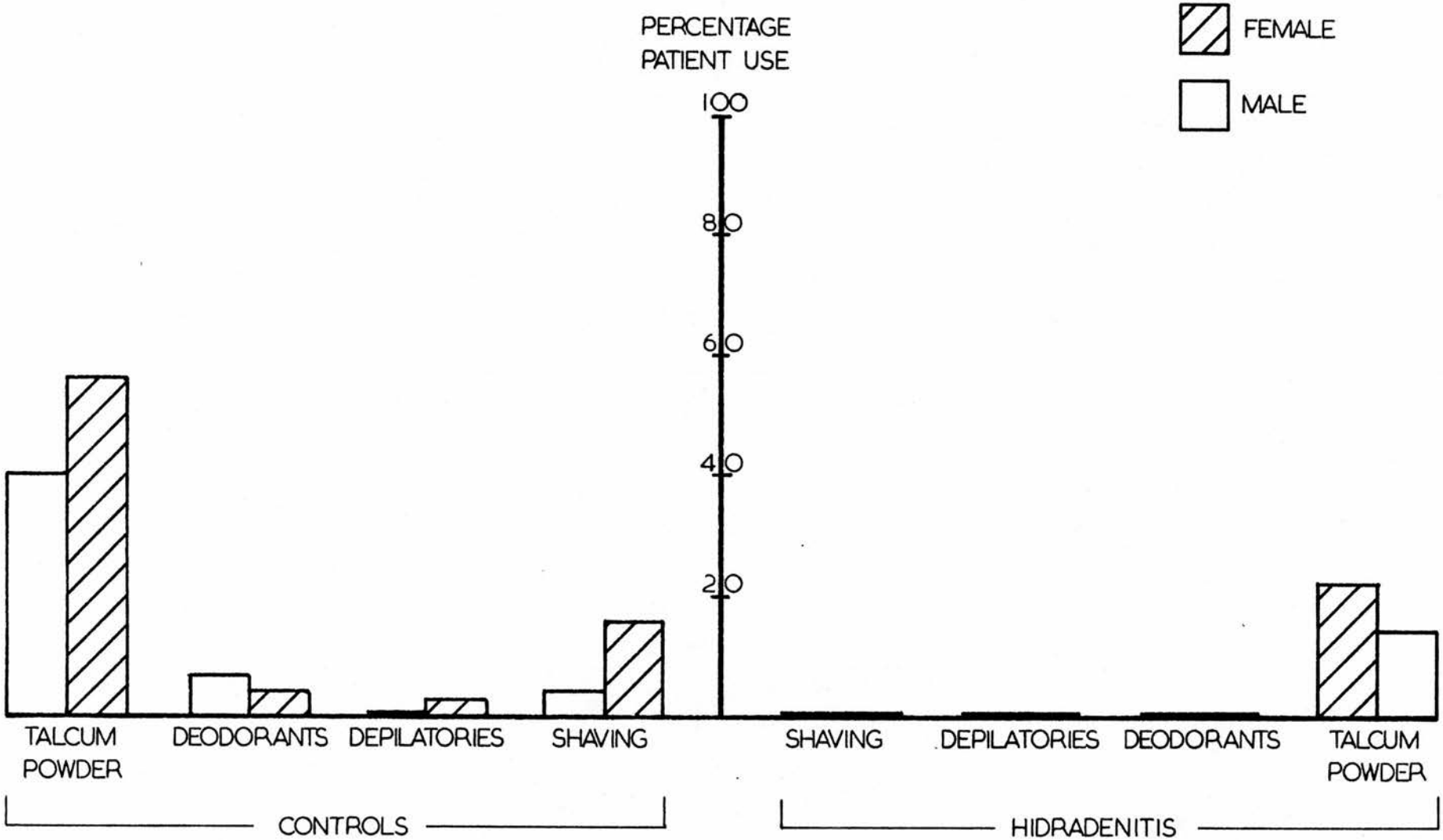


FIG. 9. HYGIENE IN THE PUBO-INGUINAL REGION



None of these differences, in either sex reached statistical significance. Significantly fewer female patients than controls had used talcum powder (x^2 test) at both sites, x^2 being 4.48, $p<0.05$ for the axilla, and $x^2 = 7.19$, $p<0.01$ in the pubo-inguinal region. The effect was similar in the males, but did not reach significance at either site.

4.8 THE INFLUENCE OF MENSTRUAL PERIODS AND PREGNANCY UPON HIRDRADENITIS

Forty-five women with hidradenitis entered the study. The results are shown in Tables 7 and 8.

Seventeen (17) of the women were nulliparous, at the time they presented for treatment of hidradenitis. Seventeen (17) women, totalling 56 pregnancies between them, had completed their pregnancies prior to the onset of hidradenitis. Eleven (11) of the 45 women had, therefore, experienced pregnancy since the onset of hidradenitis. Six of the 11 women (55%) considered that the severity of their disease had considerably abated during pregnancy; three reporting a complete disappearance of the condition during pregnancy, only to have it return soon after delivery. Three (3) of the 11 women were of the opinion that their pregnancies had no influence upon the severity of the hidradenitis, and two (2) considered that the severity of the condition had increased during pregnancy.

Four (4) of the 45 women were menopausal prior to the onset of hidradenitis. Forty-one (41) of the women had, therefore, experienced menstrual periods, while suffering from hidradenitis. Sixteen (16) of the 41 women considered that they experienced an exacerbation of hidradenitis during the week prior to their menstrual period or during the period itself. Twenty-five (25) of the women considered that their menstrual periods had no influence on the severity of the hidradenitis. None of the women reported an improvement in the severity of hidradenitis in relation to their menstrual periods. Sixteen (16) of the 45 women had taken courses of various oral contraceptive agents, while hidradenitis was present; none of these patients considered that the contraceptive pill had any

TABLE 7.

RELATIONSHIP BETWEEN PREGNANCY AND THE ACTIVITY OF HIDRADENITIS SUPPURATIVA.

TOTAL NO. OF WOMEN WITH HIDRADENITIS STUDIED IN RELATION TO PREGNANCY	= 45	
NO. OF NULLIPAROUS WOMEN	= 17 (37.8%)	
NO. OF WOMEN WHO HAD COMPLETED THEIR PREGNANCIES PRIOR TO THE DEVELOPMENT OF HIDRADENITIS	= 17	NO. OF PREGNANCIES RANGE = 1 - 7 MEAN = 3.29 MEDIAN = 3
NO. OF WOMEN WHO HAD EXPERIENCED PREGNANCY, WHILE SUFFERING FROM HIDRADENITIS	= 11 (24.4%)	
HIDRADENITIS WORSE DURING PREGNANCY	= 2/11 (18.2%)	
PREGNANCY HAD NO EFFECT ON HIDRADENITIS	= 3/11 (27.3%)	
HIDRADENITIS, BETTER DURING PREGNANCY	= 6/11 (54.5%)	

TABLE 8.

RELATIONSHIP BETWEEN SEVERITY OF HIDRADENITIS AND MENSTRUAL PERIODS.

TOTAL NO. OF WOMEN IN THE SURVEY	= 45	
NO. OF WOMEN POST-MENOPAUSAL PRIOR TO DEVELOPMENT OF HIDRADENITIS	= 4	(8.9%)
NO. OF WOMEN WHO REPORTED THAT HIDRADENITIS WAS EXACERBATED BY PERIODS	= 16/41	(39%)
NO. OF WOMEN WHO REPORTED THAT HIDRADENITIS WAS IMPROVED BY PERIODS	= 0	
NO. OF WOMEN WHO CONSIDERED THAT PERIODS HAD NO EFFECT UPON THE SEVERITY OF HIDRADENITIS	= 25/41	(61%)

influence upon the severity of their hidradenitis.

There was no correlation between the site or extent of the hidradenitis and the response to pregnancy or menstrual periods in this group of women.

In view of the exacerbation of hidradenitis in association with the menstrual periods in a substantial proportion of the women in this study, it appeared that suppression of the pituitary gonadotrophins could lead to an improvement in the severity of the disease. Four (4) women with active chronic hidradenitis were treated with the pituitary gonadotrophin suppressant, Danazol, in doses of 200 - 800 mg. daily, until menstruation was abolished. None showed improvement in the severity of hidradenitis.

DISCUSSION

4.1 HIDRADENITIS AND IRON DEFICIENCY ANAEMIA

Tennant et al. (1968) reported that ten of their forty-two hidradenitis patients had a severe iron deficiency anaemia. All ten patients had suffered from disease involving the buttocks and groins, for a minimum period of two years. The anaemia responded to surgical treatment but not to iron therapy.

There was no case of iron deficiency anaemia in this series. This suggests that no primary association exists between hidradenitis and iron deficiency anaemia. Iron deficiency anaemia occurring in these circumstances is probably of the type that occurs in many different forms of longstanding sepsis.

4.2 PREVALENCE OF DIABETES MELLITUS IN HIDRADENITIS PATIENTS AND THEIR FAMILIES

Because chronic infections are more common in patients with diabetes mellitus, the question as to whether hidradenitis patients show an increased prevalence of diabetes is relevant.

Mustafa (1980) stated that diabetes had not been shown to directly predispose to hidradenitis. Chapman (1972) found diabetes in 10% of his series of hidradenitis patients, and Bell and Ellis (1978) found a history of diabetes amongst the relatives of 12.5% of their hidradenitis patients. Mackenna (1960) described abnormal handling of glucose loads in hidradenitis.

None of the hidradenitis patients in this series were known diabetics or had symptoms of diabetes. Fifty-six of the patients did not undergo a glucose tolerance test but had fasting venous plasma glucose levels below 6.0 mmol./l. The twenty-seven patients who received a glucose tolerance test, revealed one patient who had impaired glucose tolerance, according to WHO Expert Committee on Diabetes (2nd Report) criteria.

While these findings were not compared with a similar study in a normal control population, they do not support an association

between hidradenitis and diabetes mellitus. It is, of course, possible that if all the fifty-six patients who had a fasting venous plasma glucose performed had undergone a glucose tolerance test, the prevalence of impaired glucose tolerance may have been higher.

When hidradenitis patients and controls were compared there was no significant difference in the family history of diabetes.

4.3 A COMPARISON OF THE ABO AND RHESUS BLOOD GROUPS IN HIDRADENITIS PATIENTS, AS COMPARED TO THE PROPORTION OF THOSE GROUPS IN THE NORMAL POPULATION

There were no significant differences in the proportions of ABO and Rhesus blood groups between hidradenitis patients and normal controls, thus failing to provide any evidence of a genetic transmission of disease susceptibility at this level. HLA typing of related hidradenitis patients, or families with a marked incidence of the disease, may produce more valuable results.

4.4 FAMILY HISTORY OF HIDRADENITIS SUPPURATIVA IN HIDRADENITIS PATIENTS AS COMPARED TO NORMAL CONTROLS

Little attention has been paid in the literature to the family history of hidradenitis patients. Knaysi et al. (1968) reported a family history of hidradenitis in three of eighteen patients (17%) specifically questioned. Weiner et al. (1976) in describing a patient with hidradenitis on the leg, in addition to disease at the more classical sites, reported that the patient had a strong family history of perianal abscesses. Steiner and Greyson (1955) suggested that in cases of familial hidradenitis, inherited malformation of the ducts may be relevant. In this study, 38% of the male and 24% of the female hidradenitis patients had a positive family history of hidradenitis, and this was significantly increased as compared to normal controls. Whether this positive family history reflects a genetic mechanism or is the result of sharing a common environment is difficult to determine, and requires further investigation.

4.5 THE PREVALENCE OF ACNE VULGARIS, SEBACEOUS (EPIDERMOID) CYSTS, IN HIDRADENITIS PATIENTS AS COMPARED TO A NORMAL POPULATION

The prevalence of acne vulgaris was significantly increased in both our male and female hidradenitis patients as compared to normal controls. However, our figures of 54% for males and 27% for females were lower than those reported by Steiner and Greyson, 1955 (75%) and Conway, Stark and Climo, 1952 (70%).

Knaysi et al. (1968) found an increased incidence of sebaceous (epidermoid) cysts (9%) in their series of hidradenitis patients. In our series, 39% of the male hidradenitis patients and 16% of the female hidradenitis patients had sebaceous cysts, compared to 10% of the male and 6% of the female controls. The increased prevalence of sebaceous cysts in male hidradenitis patients and hidradenitis patients as a whole, was significantly increased as compared to controls. The increased prevalence in female hidradenitis patients as compared to controls was not significant.

The association of acne vulgaris and sebaceous cysts with hidradenitis would lend support to the theory that the basic mechanism of hidradenitis is obstruction of the pilo-sebaceous unit, possibly due to hyperkeratotic plugging.

Much remains to be discovered about keratin production and dyskeratosis, Ogawa and Yoshiike (1984).

4.6 THE PREVALENCE OF HYPERSENSIVITY REACTIONS IN HIDRADENITIS PATIENTS AS COMPARED TO NORMAL CONTROLS

There were no significant differences in the prevalence of hypersensitivity reactions to antibiotics or other materials, or of the prevalence of asthma or hay fever in the hidradenitis patients as compared to normal controls. There was an increased prevalence of Elastoplast allergy in the hidradenitis patients as compared to controls. However, the difference only reached significance for the male hidradenitis patients. The prevalence of allergy

to Elastoplast, in our series, was 5% for male controls and 15% for female controls, which are higher than Smith and Nephew's figure of approximately 2%. There is little data available to form a true assessment of the prevalence of Elastoplast allergy in the general population.

In general, hidradenitis patients did not appear to be more atopic than normal controls.

4.7 THE USE OF DEPILATION, DEODORANTS AND TALCUM POWDER IN HIDRADENITIS PATIENTS, PRIOR TO THE ONSET OF THE DISEASE, AS COMPARED TO NORMAL CONTROLS

The axillary and inguinal regions are both common sites of presentation for hidradenitis suppurativa, and it would appear unlikely that mechanical shaving, chemical depilatories or deodorants, should be primarily involved in the initiation of hidradenitis, when such a marked difference in the use of these agents exists. In addition, the study previously described in this thesis showed that no significant difference existed in the use of the above agents at either site, between controls and hidradenitis patients prior to the onset of the disease. While the role of these agents as triggering factors in individuals with genetically determined disease susceptibility cannot be ruled out, these results would suggest that shaving, chemical depilatories and deodorants are not primarily responsible for the initiation of hidradenitis. With regard to deodorants alone, the experimental work of Hurley and Shelley (1960) is of interest. They demonstrated that aluminium, zirconium and cream surfactant deodorant preparations applied to one axilla daily for one week, and using the opposite axilla as a control, failed to reduce apocrine sweating in ninety normal males. In addition, histological examination of the treated axillae failed to reveal any changes in the apocrine secretory cells, ducts or stratum corneum; other skin structures were also normal.

The finding of a significantly increased use of talcum powder in the axillary and pubo-inguinal regions of female controls is difficult to explain. However, it makes it unlikely that the use of talcum

powder causing obstruction of the pilo-sebaceous follicles is involved in the aetiology of hidradenitis suppurativa.

4.8 THE INFLUENCE OF MENSTRUAL PERIODS AND PREGNANCY UPON HIDRADENITIS

Anderson and Dockerty (1958), Hurley and Shelley (1960) and Harrison (1964) reported exacerbations of hidradenitis in some of their patients pre-menstrually. Cornbleet (1952b), reported an improvement in the severity of hidradenitis and Fox-Fordyce disease in some of his patients during pregnancy. In this series, sixteen out of forty-one women reported an exacerbation of their disease pre-menstrually, and approximately half of the women, who had experienced a pregnancy during the course of the disease, reported an improvement in their condition. The remainder of the women, considered that neither menstrual periods nor pregnancy influenced the severity of their disease.

There is not, therefore, a definite relationship between menstrual periods and pregnancy and the activity of hidradenitis. However, the results obtained suggest that the fluctuation in the levels of sex hormones does exert some effect upon the activity of hidradenitis, probably at the level of the pilo-sebaceous unit.

No consistent alteration in hormone levels have been described in hidradenitis, and none of the available hormones, known to be increased during pregnancy, have been of any value when administered to patients with hidradenitis, Cornbleet (1952a). Certainly, in our study, those women who had taken the contraceptive pill while suffering from hidradenitis had not noticed any effect upon the activity of the disease, and the use of Danazol also failed to influence the activity of hidradenitis.

Brunsting (1952) suggested that an excess of androgen may play an important part in the aetiology of hidradenitis. However, Cornbleet (1952a) reported an improvement in a group of women with hidradenitis and Fox-Fordyce disease, treated with testosterone-propionate.

It is possible that the mechanism of hormone action in hidradenitis may parallel that of acne vulgaris. Recent work, Darley (1984), suggests that while persistently elevated levels of circulating androgens may explain some cases of acne, it is more likely that an abnormality in end organ sensitivity is the cause in the majority of patients. That the pilo-sebaceous unit is a versatile organ of androgen metabolism has been shown by Takayasu (1979). Androgens such as dehydroepiandrosterone may be converted to the more potent testosterone, which in turn may be converted to dihydrotestosterone, the most potent androgen known. The enzyme necessary for this conversion, 5 alpha-reductase is also present in skin. Dihydrotestosterone attaches to a cytosol androgen receptor protein, and this complex is transferred to the nucleus (Takayasu 1979). An increase in receptor protein concentration, or an increase in its affinity or more rapid transfer of the complex to the nucleus, would all serve to increase the local effect of androgen on the pilo-sebaceous unit; a change which would not be discovered by systemic studies.

SECTION C.

STUDIES OF THE APOCRINE GLANDS IN HIDRADENITIS SUPPURATIVA

CHAPTER V

THE SURFACE AREA, DIAMETER AND NUMBERS OF THE APOCRINE GLANDS IN HIDRADENITIS SUPPURATIVA

CONTENTS PAGE

SURFACE AREA, DIAMETER AND NUMBER OF APOCRINE GLANDS IN THE AXILLA AND PUBO-INGUINO-PERINEAL AREA

INTRODUCTION

5.

The reports of Shelley and Cahn (1955), Spiller and Knox (1958) and Stone (1976) support the concept that the basic mechanism in hidradenitis is hyperkeratotic plugging of the apocrine duct, followed by duct dilatation and superinfection. However, nobody to date has ascertained whether the apocrine sweat glands differ in numbers, size or in quantity in hidradenitis patients as compared to normal subjects. This chapter describes a study of the surface area, diameter and number of the apocrine glands in the axillae and in the pubo-inguino-perineal region of hidradenitis patients and normal subjects, and compares the values obtained in the axilla with those of hyperhidrosis patients.

PATIENTS AND METHODS

5. SURFACE AREA, DIAMETER AND NUMBER OF APOCRINE GLANDS IN THE AXILLA AND PUBO-INGUINO-PERINEAL AREA

In order to compare the surface area, diameter and numbers of apocrine glands, one cm^2. of skin was excised from the apex of the hairy area of the axilla in 32 hidradenitis patients (23 female and 9 male), 10 hyperhidrosis patients (4 female and 6 male), and 17 control patients (12 female and 5 male). As it was necessary for the purposes of comparison to define a standard site for biopsy, the apex of the hair growing part of the axilla was chosen as an easily definable apocrine gland containing area in that region, Fig. 10.

The 10 hyperhidrosis samples were obtained from patients who were undergoing axillary excision for excessive sweating and who were of a similar age to the hidradenitis patients. The 17 control samples were obtained from patients without hidradenitis, of a similar age range to the hidradenitis patients. Since, the hairy area of the axilla is not commonly entered during routine surgical procedures, control samples of this area were obtained from the lateral ends of extended oblique mastectomy incisions and from axillary node biopsies.

It was difficult to select a representative area for the pubo-inguino-perineal region, as the exact distribution of the apocrine glands in this region has not been previously defined. The skin over the pubic tubercle was chosen as the defined point in the pubo-inguino-perineal region because this landmark can be easily felt, and being closely related to the pubic hair, was likely to have overlying skin that contained apocrine glands. One cm^2. of skin from this site was obtained in 18 hidradenitis patients (14 female and 4 male) undergoing radical excisions for pubo-inguino-perineal disease. Seventeen (17) control samples (12 female and 5 male) taken from over the pubic tubercle were obtained from patients undergoing repair of an inguinal hernia or laporotomy via a lower paramedian incision.

Vertical sections were cut at one millimetre intervals through

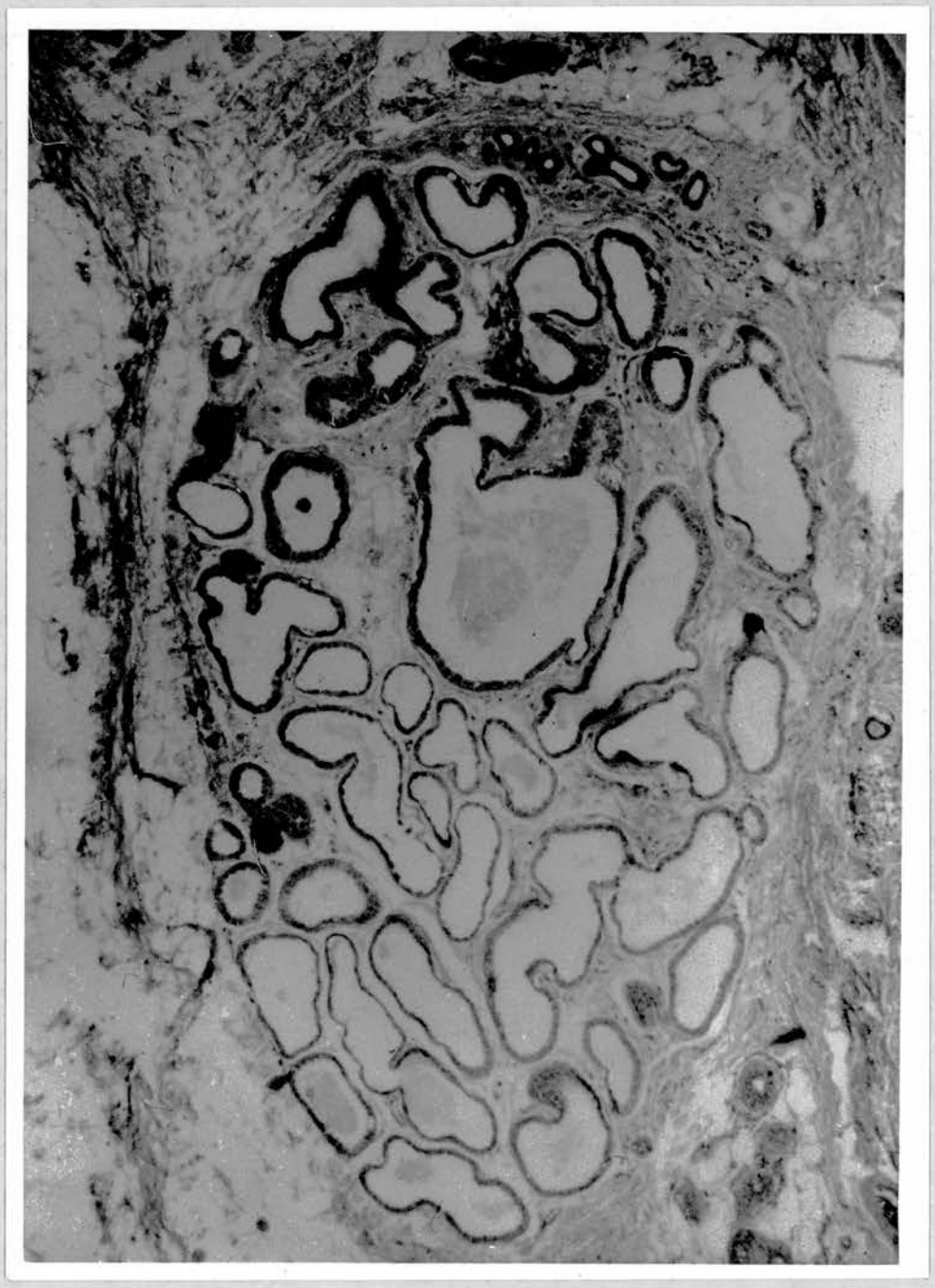


FIG. 10. AXILLARY APOCRINE SWEAT GLAND.

the one cm^2. of skin, resulting in 10 sections in all. The sections were stained with haematoxylin and eosin (H. & E.) and mounted on a gridded slide for light microscopy.

The density of the apocrine glands in the skin samples were determined by counting the numbers of apocrine glands per 10 sections from each sample and the result expressed as glands/cm^2. The grid was used to separate one microscopic field from another. An index of the size of the apocrine glands was obtained by measuring the diameters of the largest apocrine gland in each of the 10 sections; the microscope having been fitted with a previously calibrated scale for that magnification. The largest diameter measured per 10 sections was then taken as an index of the size of the apocrine glands in that sample. The rationale behind this latter concept, was that if the apocrine glands were considered to be nearly spherical, sectioning would result in less than maximal gland diameter in most instances, and that being the case, the maximum diameter measured was most likely to represent the true apocrine gland diameter.

The third parameter measured was the total surface area of the apocrine tubules in the 10 sections. A modified form of planimetry was used for this purpose, utilising the Quantimet 70 (Cambridge Instruments Ltd.), Fig. 11. The section to be studied was placed under the microscope of this instrument, which transmitted the image of the section on to a television screen. The margins of the apocrine tubules were then marked out on the screen with a light pencil, from which the Quantimet 70 calculated the surface area in terms of picture points, which were converted to millimetres squared, Fig. 12.

Difficulty was sometimes experienced in assessing the first 2 parameters accurately, i.e. the number of apocrine glands/cm^2. and the maximum diameter of the apocrine glands. This occurred when there was near confluence of the apocrine tubules in some of the axillary specimens. This made the decision as to where one gland ended and another began a difficult one. The width of the connective tissue partitions between glands and the height

FIG. 11. QUANTIMET 70.

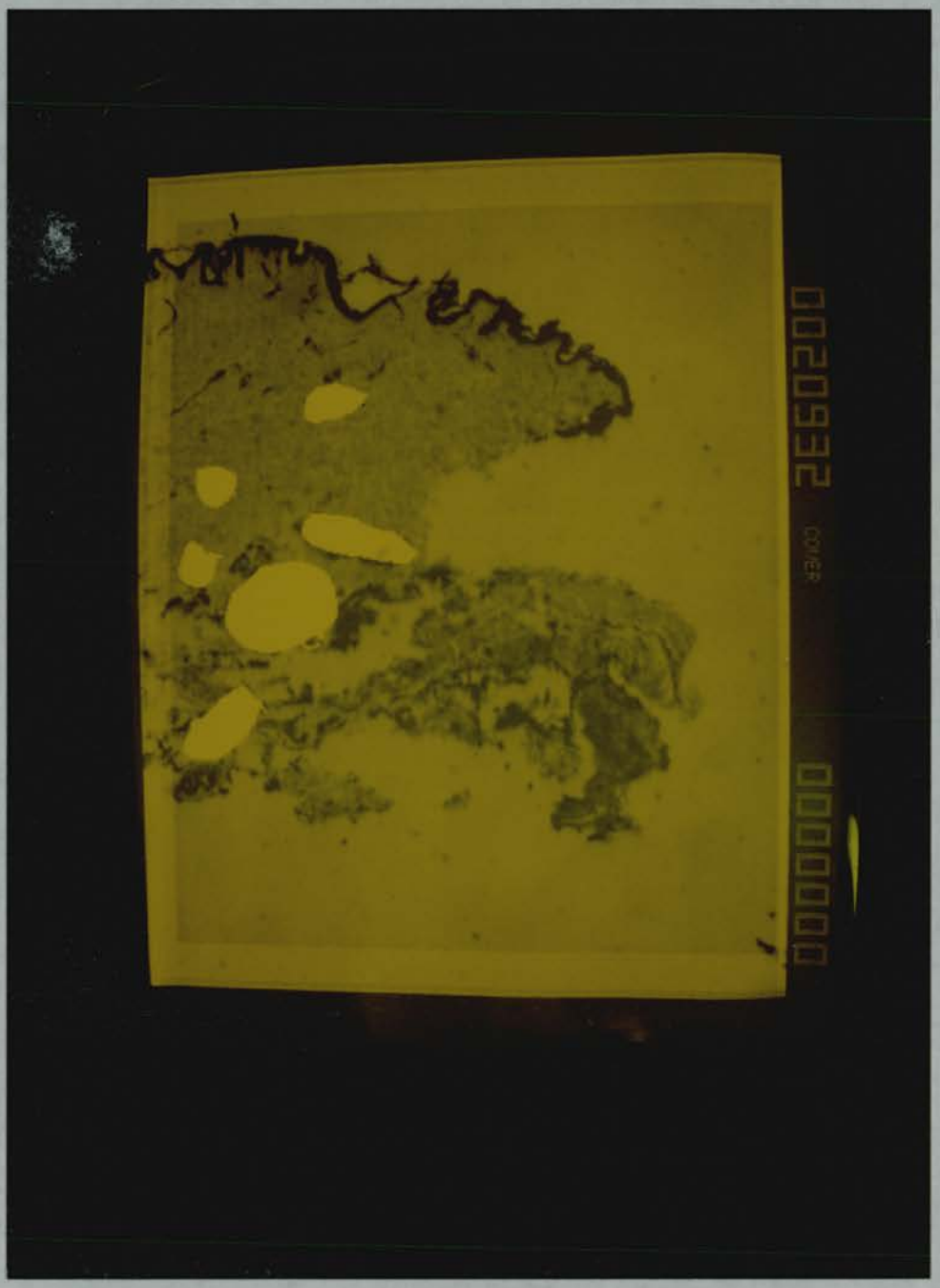


FIG. 12. APOCRINE GLANDS MARKED OUT ON SCREEN OF QUANTIMET 70.

of the tubular epithelium were used to define the limits of a unit gland, since although the epithelium may be columnar, cuboidal or squamous, the height of the cells lining the tubules of an individual apocrine gland tend to be constant. Measurement of the total surface area of the apocrine tubules using the Quantimet 70 presented no problem from subjectivity and in the latter half of the study this parameter alone was used as the index of the amount of apocrine gland tissue present in the skin of hidradenitis, hyperhidrosis and control patients.

RESULTS

5. SURFACE AREA, DIAMETER AND NUMBER OF APOCRINE GLANDS IN THE AXILLA AND PUBO-INGUINO-PERINEAL AREA

The numbers of apocrine glands/cm^2., their maximum diameters and the total surface area of the apocrine tubules in the axillae of hidradenitis, hyperhidrosis and control subjects are shown in Appendices 4, 5 and 6. The median, mean $\pm$ standard deviation values and ranges are shown in Table 9. If the 2 subjects with extensive axillary fibrosis were excluded from the hidradenitis group as being unrepresentative of the centre of that axilla, the values for the surface area of the apocrine tubules in the hidradenitis group became 31.99 mm^2. (median), 40.34 $\pm$ 25.95 mm^2. (mean $\pm$ SD) and 7.1 to 92.3 mm^2. (range).

Comparison of the results was performed using the two tailed Mann-Whitney U test. The number of apocrine glands/cm^2. did not differ significantly between the 3 groups ($p > 0.1$). The maximum diameter of the apocrine glands in hyperhidrosis was significantly increased as compared to that of the glands in controls ($p < 0.002$) and in hidradenitis subjects ($p < 0.05$). The surface area of the apocrine glands in hyperhidrosis was, also, significantly greater than those in normal controls ($p < 0.002$) and hidradenitis patients ($p < 0.001$). Both in terms of gland diameter and surface area, the results obtained for controls and hidradenitis patients did not differ significantly. These results were not altered if the 2 hidradenitis patients showing extensive fibrosis were excluded from the study. The sexes in each of the 3 groups were not compared separately, because of the small numbers in some sub-groups.

Apocrine glands were only seen in 5 of the 18 samples taken from over the pubic tubercle in hidradenitis subjects, and in 5 of the 17 samples from the control group. No apocrine glands could be visualised in the other samples, although hair follicles, eccrine sweat glands and sebaceous glands were not uncommon. The results are shown in Appendices 7 and 8.

The mean, median and range of values for the measured parameters in those samples positive for apocrine glands are given in Table 10.

TABLE 9. RANGE, MEAN AND MEDIAN VALUES FOR NUMBERS OF GLANDS/CM^2., GLAND DIAMETER, AND SURFACE AREA IN AXILLARY SAMPLES.

VALUE	HYPERHIDROSIS	HIDRADENITIS	CONTROLS
RANGE			
NOS. GLANDS/CM^2.	37 - 165	38 - 129	50 - 104
GLAND DIAMETER	2.69 - 2.93	1.5 - 3.6	1.5 - 2.7
SURFACE AREA	32.1 - 144.8	2.9 - 92.3	6.7 - 63.6
MEAN $\pm$ SD			
NOS. GLANDS/CM^2.	100 $\pm$ 40.3	79.86 $\pm$ 29.17	66.8 $\pm$ 17.3
GLAND DIAMETER	2.83 $\pm$ 0.14	2.52 $\pm$ 0.57	2.2 $\pm$ 0.38
SURFACE AREA	89.97 $\pm$ 40.0	38.05 $\pm$ 26.6	32.8 $\pm$ 15.9
MEDIAN			
NOS. GLANDS/CM^2.	99.5	75	62
GLAND DIAMETER	2.8	2.5	2.4
SURFACE AREA	100.6	28.3	32.8

TABLE 10. EXAMINATION OF THE SKIN OVER THE PUBIC TUBERCLE FOR APOCRINE GLANDS, IN HIDRADENITIS AND CONTROL SUBJECTS.

PARAMETERS	CONTROLS n = 17	HIDRADENITIS n = 18
NO. OF SAMPLES POSITIVE FOR APOCRINE GLANDS	5	5
RANGE		
NOS. GLANDS/CM^2.	1 - 10	1 - 20
GLAND DIAMETER	0.6 - 1.4	0.9 - 1.6
SURFACE AREA	0.16 - 2.97	1.1 - 6.9
MEAN $\pm$ SD		
NOS. GLANDS/CM^2.	3.8 $\pm$ 3.25	9.8 $\pm$ 7.7
GLAND DIAMETER	0.92 $\pm$ 0.32	1.38 $\pm$ 0.25
SURFACE AREA	1.09 $\pm$ 1.14	3.42 $\pm$ 2.43
MEDIAN		
NOS. GLANDS/CM^2.	2	5
GLAND DIAMETER	0.8	1.5
SURFACE AREA	1.06	2.85

In view of the small numbers of samples positive for apocrine glands, no firm conclusions can be drawn as to whether there are significant differences in the numbers, diameter or surface area of the apocrine glands in the skin from over the pubic tubercle, when hidradenitis and control subjects are compared. However, it would appear unlikely that any major difference exists.

DISCUSSION

5. SURFACE AREA, DIAMETER AND NUMBER OF APOCRINE GLANDS IN THE AXILLA AND PUBO-INGUINO-PERINEAL AREA

The results obtained showed no difference in the numbers of glands, diameter of glands or surface area of the apocrine tubules/cm^2. in hidradenitis and normal subjects. This has not been previously reported in the literature. This suggests that there are no gross differences in the apocrine glands in diseased and normal subjects. It does not exclude differences in the micro-architecture of gland and duct, cellular components, or intra-cellular structure, and the review of the literature suggests that these finer aspects have yet to be investigated.

The finding of an increased apocrine gland diameter and an increased surface area of apocrine tubules/cm^2. in hyperhidrosis as compared to hidradenitis and controls was a surprising result, which has not been previously reported. Hyperhidrosis is usually considered to be due to excessive function of the eccrine sweat glands. It would appear that the apocrine glands in hyperhidrosis are being subjected to some form of maximal stimulation, resulting in the full expression of their growth potential. The form of this stimulus remains unknown.

In the pubo-inguino-perineal region, apocrine glands were only found in 5/18 and 5/17 samples taken from over the pubic tubercle, in hidradenitis and controls respectively. The numbers involved were too small to enable any conclusions to be made, but no gross differences were apparent.

In retrospect, using the information obtained from the histological mapping of the apocrine glands in the pubo-inguino-perineal region of hidradenitis patients (vide infra), it would have been more rewarding to have chosen the skin of the medial portion of the flexural crease of the groin, as the standard site for sampling. This was an area where apocrine glands were consistently found in both sexes. A control sample of skin could have been obtained from patients undergoing a Trendelenberg top tie of the long saphenous vein for varicosities. The age and sex distribution would, also have been suitable.

CHAPTER VI

A METHOD OF PRE-OPERATIVELY MAPPING THE DISTRIBUTION OF THE APOCRINE GLANDS

CONTENTS PAGE

A METHOD OF PRE-OPERATIVELY MAPPING THE DISTRIBUTION OF THE APOCRINE GLANDS

INTRODUCTION

6.

This chapter describes a technique developed by the author to map the distribution of the apocrine glands in the axillae and pubo-inguino-perineal region. Many authors have expressed the opinion that the apocrine gland containing skin of an affected region must be excised completely if the condition is to be cured. However, this is difficult to achieve when the exact anatomical distribution of the apocrine glands is not known in general, or specifically in the individual affected by hidradenitis. While, anatomical features, such as the distribution of axillary and pubic hair give an approximate guide to the extent of the excisions to be carried out in these areas, they do not define clearly the exact limits of excision. A simple method of demonstrating the distribution of the apocrine glands, would therefore facilitate their complete excision.

METHOD

6.

It appeared that the most suitable method of demonstrating the apocrine glands pre-operatively would be to stimulate selectively apocrine sweating and then demonstrate the distribution of the apocrine sweat droplets. Since it is considered that keratinous plugging of the hair follicles and apocrine ducts is present in hidradenitis, the success of the above method would depend on some of the apocrine glands remaining patent.

Hurley and Shelley (1960) demonstrated that adrenalin and oxytocin would stimulate the expulsion of apocrine sweat on to the skin surface. They administered small doses of adrenalin intracutaneously and apocrine sweating was observed in the area of the raised wheal. It was considered that a systemic dose of adrenalin sufficient to produce generalised apocrine sweating would produce unpleasant and dangerous side effects. For this reason oxytocin was used.

It was ascertained prior to the procedure, that the patient was normotensive and was not pregnant. The skin of the region under study was shaved 48 hours prior to the procedure. (This was considered advisable as firm stroking of the skin can express apocrine sweat and apocrine glands have a refractory period of 24 - 48 hours after emptying, Hurley and Shelley (1960). Atropine (1.2 mg.) was given intravenously to block eccrine sweating. The skin was cleansed with alcohol, and a 2% alcoholic iodine solution applied to the area under study and to the palm of the hand. When dry, a mixture of 75g. of fine starch powder in 100 mls. of castor oil was applied to these areas. Oxytocin (2i.u.) was given slowly intravenously. Within 3 - 5 minutes the black spots of apocrine sweat could be seen at follicular sites and occasionally at extra follicular sites. The palm of the hand acted as a control to ensure that eccrine sweating had been completely blocked by the atropine, since the palmar skin contains numerous eccrine but no apocrine glands. The procedure was terminated if there was any appearance of sweating on the palm, Fig. 13.

FIG. 13. PALM OF HAND COATED WITH IODINE AND STARCH.
ECCRINE SWEATING BLOCKED WITH ATROPINE.

At the end of the above procedure, the result was photographed and the area in which apocrine sweating had been demonstrated was marked out with a skin pencil for excision.

RESULTS

6.

The atropine/iodine/starch and oxytocin method was used to demonstrate the distribution of the apocrine glands in 40 axillae (30 female and 10 male), and in 18 pubo-inguino-perineal regions (12 female and 6 male).

The sweat droplets appeared as small black dots, situated mainly around the stumps of the regional hair, but occasionally at extra-follicular sites, (the apocrine ducts can occasionally open directly on to the skin surface, Hurley and Shelley 1960). The droplets were necessarily small, as the amount of sweat produced by one apocrine gland is only 0.001 ml.

In the axillae, Figs. 14 and 15, numerous droplets were present in the hair growing area. However, droplets in a variable and decreasing density could extend for 2 - 3 cm. outside this zone. In one male patient, in particular, the droplets continued in a very scattered low density pattern from his axillae over the anterior aspect of his chest.

In the pubo-inguino-perineal area, the droplets were concentrated in the skin of the medial portions of the flexural creases of the groins and adjacent upper thighs, extending posteriorly towards the anus. In the female, they were particularly marked on the external aspects of the labia majora, Figs. 16 and 17. The iodine and starch mixture was not applied to the inner aspects of the labia majora or the minora, and it is not possible to comment upon these areas. In the male, droplets were seen around the root of the penis and at the junction of the scrotal skin and groin, Fig. 18. In both sexes, droplets appeared over the pubic skin, and extended in a scattered and variable extent over the lower abdomen. In some patients there was a concentration of droplets in the peri-umbilical area.

The atropine/iodine/starch and oxytocin method was also used in the 4 patients undergoing excision of the skin over the sternum and in the 2 patients undergoing excision of the inframammary

FIG. 14. APOCRINE SWEATING IN THE AXILLA.

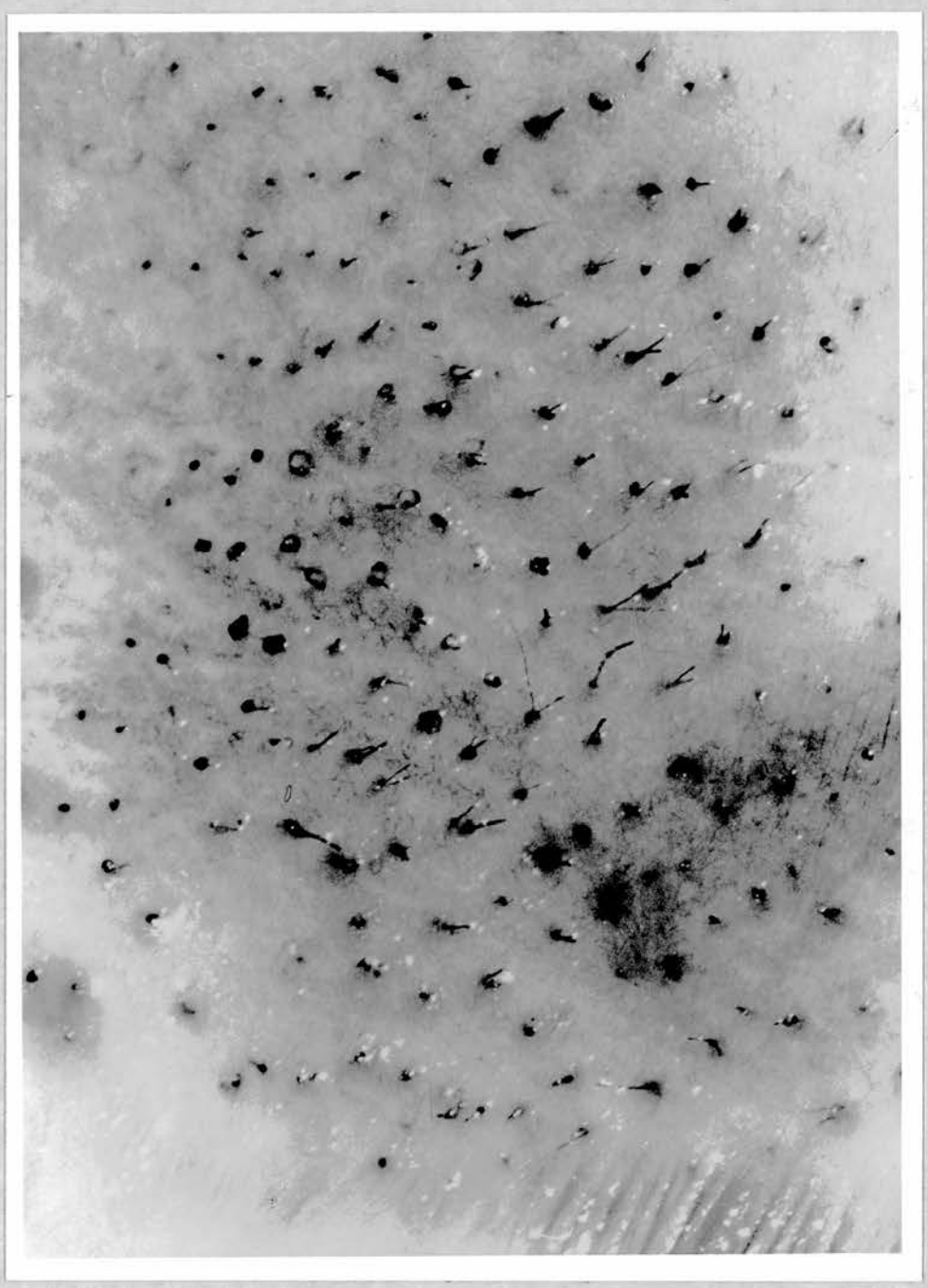


FIG. 15. APOCRINE SWEAT DROPLETS IN THE AXILLA.

FIG. 16. APOCRINE SWEATING IN THE FEMALE PUBO-INGUINO-PERINEAL REGION.

FIG. 17. APOCRINE SWEAT DROPLETS IN THE FEMALE PUBO-INGUINO-PERINEAL AREA.

FIG. 18. APOCRINE SWEATING IN THE MALE PUBO-INGUINO-PERINEAL REGION.

folds of the breasts. In no case did it reveal a concentration of apocrine glands in these areas.

DISCUSSION

6.

The distribution of the sweat droplets as demonstrated by the atropine/iodine/starch and oxytocin method, in the absence of palmar eccrine sweating, correlated well with the histological distribution of the apocrine glands in the same piece of skin, studied following its excision.

In practical terms, the atropine/iodine/starch and oxytocin method made little difference to the extent of the axillary excisions performed. This is undoubtedly because the apocrine glands, themselves, are closely related to the distribution of the regional hair, as were the excisions prior to the use of the method. As will be seen from the microscopy of the peripheries of the excised axillary specimens, all apocrine glands were still not excised, despite the pre-operative use of the atropine/iodine/starch and oxytocin method, Chapter VII. This is probably because a very scattered low concentration of apocrine glands extends outside the main concentration of apocrine glands, and these were not included in the area marked out for excision. However, the presence of a few isolated apocrine glands at the margins of excision does not appear to have led to a significant recurrence rate, Chapter IX.

The distribution of the apocrine sweat droplets in the pubo-inguino-perineal region led to a standardised pattern of excision in this area, which is described in Chapter IX. It was not practical to include the apocrine glands that extended in an isolated scattered fashion over the abdomen, in this excision.

CHAPTER VII

THE DISTRIBUTION OF THE APOCRINE GLANDS

IN THE AXILLA AND PUBO-INGUINO-PERINEAL REGION

CONTENTS PAGE

CONTENTS PAGE

INTRODUCTION

This chapter details the microscopic studies carried out to demonstrate the distribution of the apocrine glands in the axilla and pubo-inguino-perineal region. The distribution of the glands as shown by microscopy was used to confirm their distribution as demonstrated pre-operatively by the atropine/iodine/starch and oxytocin method.

PATIENTS AND METHODS

7.1 MICROSCOPIC STUDY OF AXILLARY SPECIMENS

Following the use of the iodine/starch and oxytocin method and excision of the axillary skin; the specimens obtained were studied by 3 methods.

7.1.1 SAMPLING OF THE PERIPHERY OF AXILLARY SPECIMENS

Eighteen formalin fixed specimens, obtained at radical excision of the axilla for hidradenitis, were studied to determine the relationship between the size of the excision and the extent of remaining apocrine tissue at the margins of the excised skin. The 2 maximum diameters, (measured at right angles to one another through the centre of the specimen) were measured in centimetres. The product of the 2 diameters was taken as an index of the size of the excised skin. Samples of skin were then taken from sites around the periphery of the specimen and 3 vertical sections cut from each sample, resulting in a total of 159 blocks and 477 sections. The sections were stained with haematoxylin and eosin and examined microscopically for the presence of apocrine glands.

7.1.2 SAMPLING OF AXILLARY SPECIMENS FROM THE PERIPHERY TO THE CENTRE

Twelve excised axillary specimens were studied in greater detail. Eight radii, approximating the points of a compass were drawn through the specimen. Commencing at the periphery of the specimen, one cm^2. samples were taken along the 8 radii, at one centimetre intervals, until the final block was taken from the centre of the specimen (Fig. 19). Ten vertical sections, at one millimetre intervals were cut from each sample, and after staining with H. and E., each section was examined using the Quantimet 70. The surface area of the apocrine tubules were calculated in mm^2. for the peripheral specimens as a whole, and the same exercise was carried out at one centimetre intervals until the central sample was reached. By dividing the total surface area of the peripheral samples, or intermediate samples by 8 (for the number of radii), it was possible to compare the mean surface area of

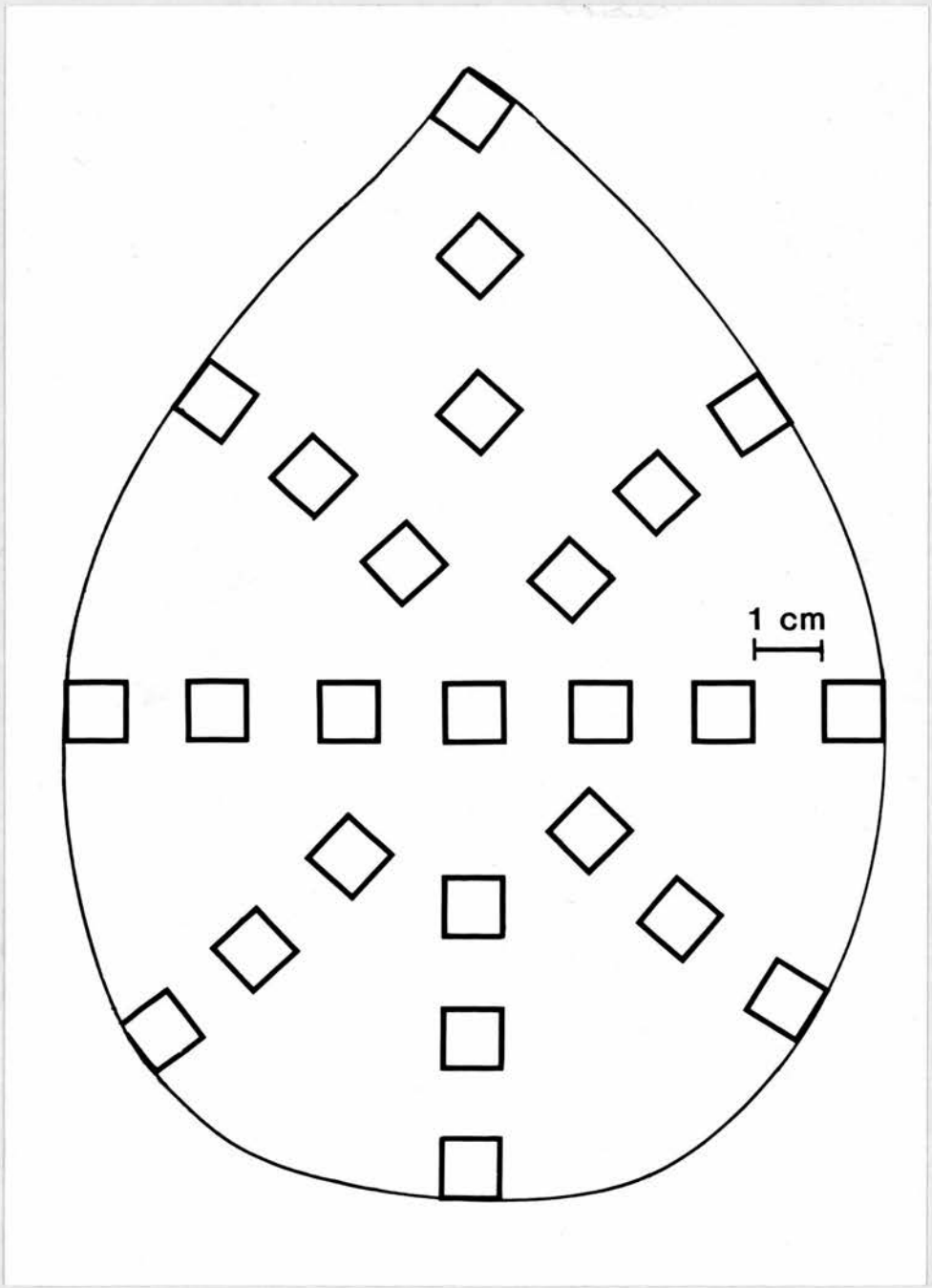


FIG. 19. METHOD OF RADIAL SAMPLING OF AXILLARY SKIN.

the apocrine tubules in the peripheral or intermediate samples with the single central sample.

7.1.3 MICROSCOPIC STUDY OF WIDELY EXCISED CADAVERIC AXILLARY SPECIMENS

Wide excisions of axillary skin was performed in 3 cadavers, who had not experienced disease or surgery in relation to the axilla. The specimens obtained were studied by the same technique as described in section 7.1.2.

7.2 THE DISTRIBUTION OF THE APOCRINE GLANDS IN THE PUBO-INGUINO-PERINEAL REGION

Following radical surgery for pubo-inguino-perineal hidradenitis, the excised skin specimens consisted of the skin from over the symphysis pubis and the adjacent hypogastric skin; the skin over the medial halves of the groins and the adjacent upper thighs; plus in the female, the skin of the external aspects of the labia majora and in the male, the adjacent 1 - 2 cm. of scrotal skin.

The excised skin was studied by microscopy in 3 different fashions:-

7.2.1 Samples were taken from the edge of 5 excised pubo-inguino-perineal specimens (4 female and one male) and their position recorded by photography. After preparation and staining with H. & E. they were examined for the presence of apocrine glands. When apocrine glands were found, their position was recorded at the appropriate position on the photograph.

7.2.2 Four (4) female pubo-inguino-perineal specimens were blocked in their entirety, using parallel vertical and horizontal incisions. Three (3) male pubo-inguino-perineal specimens were prepared in the same manner, but only half of the specimen was blocked i.e. one groin and its adjacent abdominal, thigh, perineal, scrotal and pubic skin. The male specimens were much larger than the female specimens. Each block was numbered so that its position on the photographed specimen could be identified. Three sections were

cut from each block and after staining with H. & E., were examined microscopically for the presence of apocrine glands. The presence of apocrine glands in a block was recorded by marking a cross on the photograph of the skin specimen at the point the block had been taken from. In this way, a map of the apocrine glands in this region was drawn up; Fig. 20.

7.2.3 Where the disease involved a single, well localised area in the pubo-inguino-perineal region, usually the groin, a wide local excision of that area only was performed. Three such specimens were blocked and examined microscopically for the presence of apocrine glands.

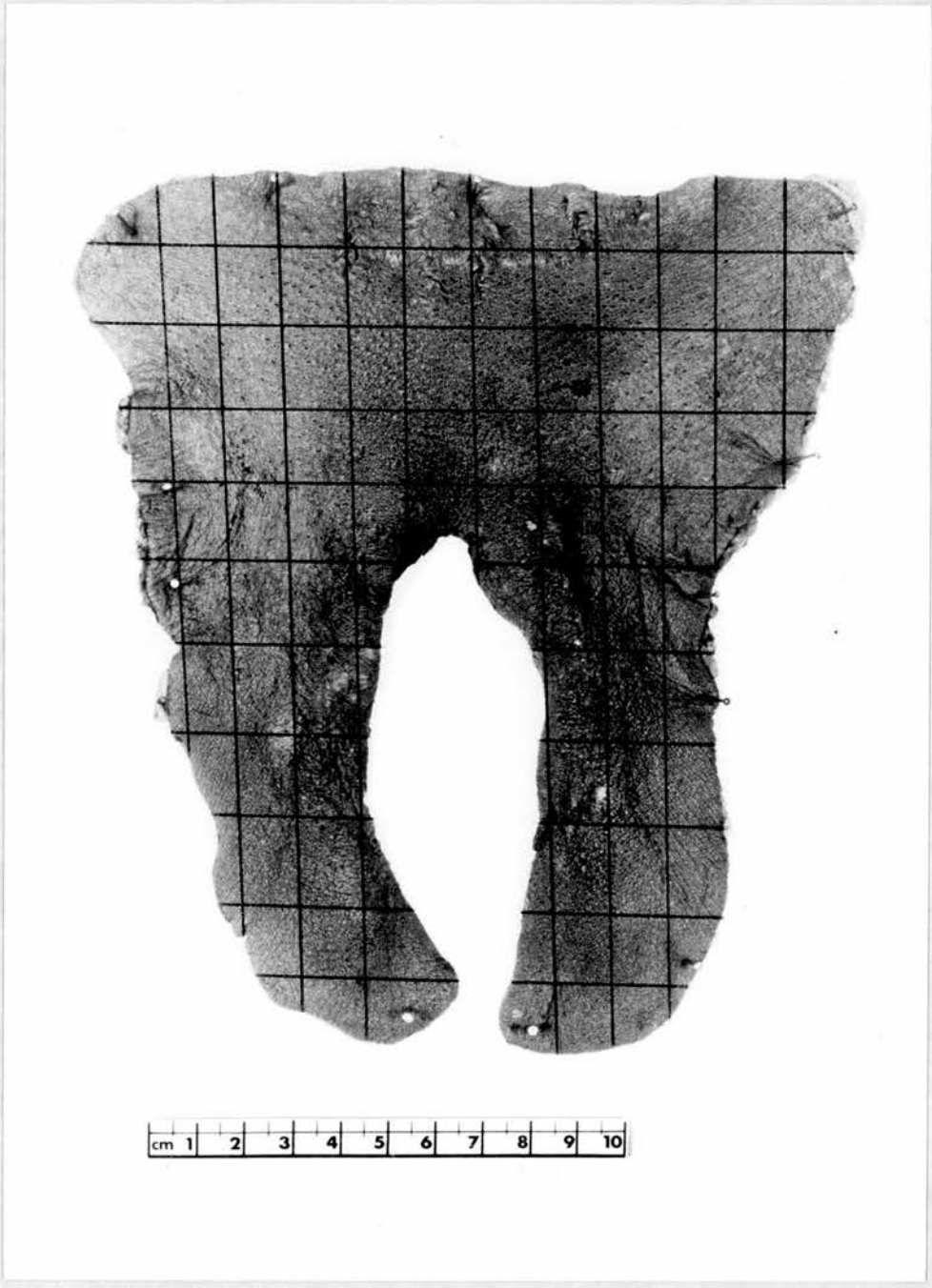


FIG. 20. BLOCKING OF PUBO-INGUINO-PERINEAL SKIN.

RESULTS

7.1.1 SAMPLING OF THE PERIPHERY OF AXILLARY SPECIMENS

The presence of apocrine glands in the blocks taken from the periphery of the axillary specimens, in relation to the size of the excised specimens are shown in Table 11.

In general, it can be seen that the dimensions of the axillary skin excised at operation in the male were greater than in the female. This probably reflects the larger size of the males. The percentage of blocks that contained apocrine glands can be plotted against the products of the aximum diameters of the excised specimens, in the form of an exponential curve, according to the formula $y = ae^{bx}(a\ o)$. This gives an r^2 value of 0.62, where 'r' is the correlation coefficient, Fig. 21. In order to test the significance of the correlation coefficient, the 't' test can be used in the formula $t = \frac{n-2}{1-r}2$, where 'r' is the correlation coefficient and 'n' is the 18 pairs of data contained in Table 11. The result shows the correlation coefficient to be highly significant, $p < 0.001$. The same holds true if a linear regression line is constructed. This suggests that the larger the excision, the surgeon performs, the more likely is the complete clearance of the apocrine glands. The margins were completely clear in only one axillary specimen.

7.1.2 SAMPLING OF AXILLARY SPECIMENS FROM THE PERIPHERY TO THE CENTRE

The results are shown in Table 12a. The table shows the total surface area of the apocrine tubules for the 8 samples taken from the periphery, for the 8 samples taken at a given distance from the periphery, and for the single central sample. The figures given in parentheses for periphery, 1 cm. in, 2 cm. in etc. represent the mean surface area of that ring i.e. the total surface area of the ring, divided by 8, for the number of radii. The mean surface area of the apocrine tubules in each ring can then be compared with that of the other rings and the single central sample. It can be seen that it was rarely possible to obtain samples for 3 and 4 cms. in, as these were limited by the smallest diameter of the skin specimen.

TABLE 11.

SAMPLING FOR THE PRESENCE OF APOCRINE GLANDS
AT THE PERIPHERY OF RADICALLY EXCISED AXILLARY SKIN
n = 18

SEX	NO. OF BLOCKS TAKEN	NO. OF BLOCKS CONTAINING APOCRINE GLANDS	% OF BLOCKS CONTAINING APOCRINE GLANDS	SIZE OF EXCISION CM^2
FEMALE	8	0	0	84
FEMALE	9	1	11	115
FEMALE	10	2	20	77
FEMALE	9	3	33	96
FEMALE	10	4	40	54
FEMALE	9	4	44	140
FEMALE	8	4	50	48
FEMALE	12	6	50	104
FEMALE	7	4	57	42
FEMALE	8	5	63	38
FEMALE	7	5	71	42
FEMALE	8	6	75	35
MALE	10	1	10	160
MALE	10	1	10	150
MALE	9	1	11	189
MALE	9	1	11	150
MALE	8	1	13	104
MALE	8	3	38	96

FIG. 21. PERIPHERAL AXILLARY BLOCKS POSITIVE FOR APOCRINE GLANDS

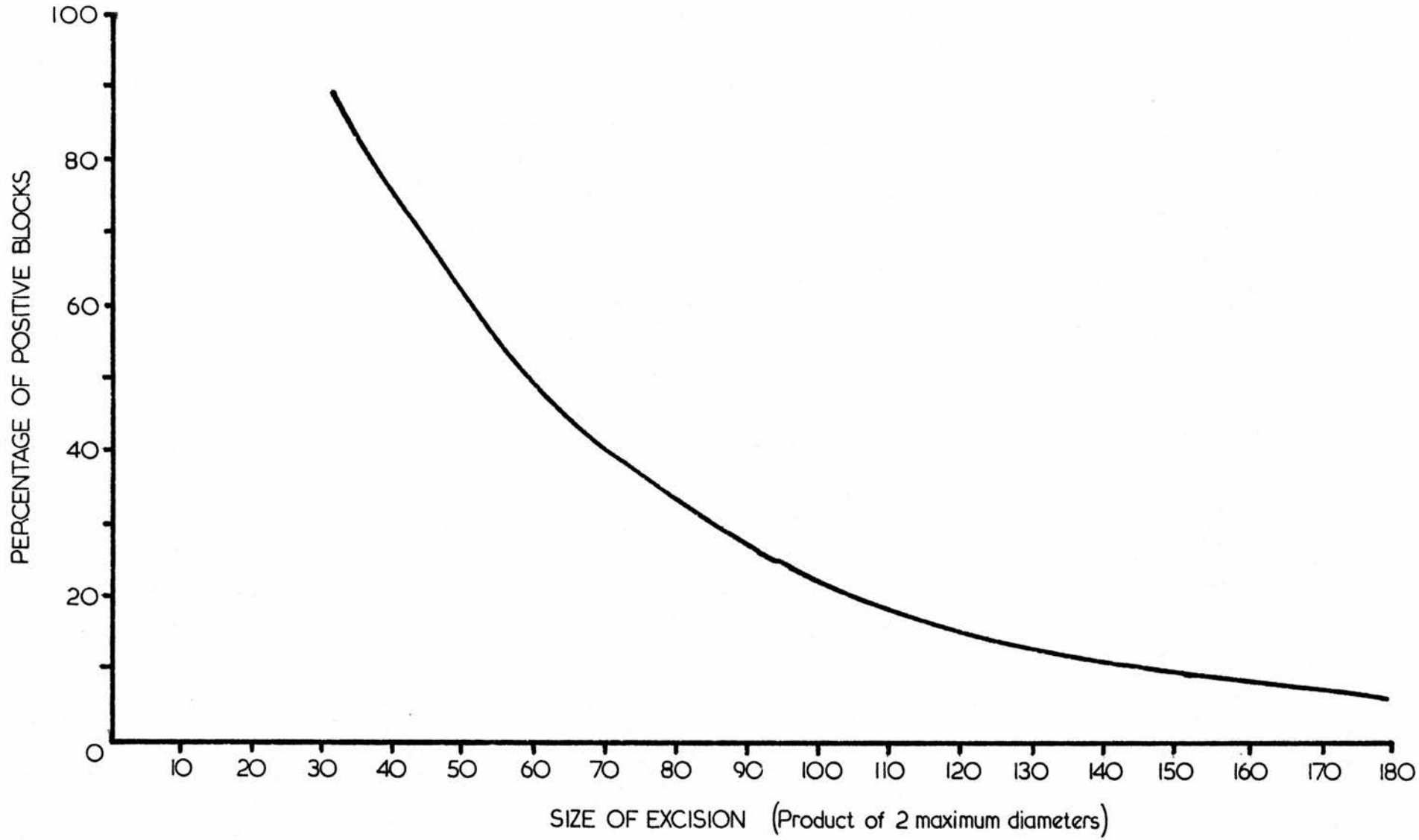


TABLE 12a. SURFACE AREA OF APOCRINE TUBULES, FROM THE PERIPHERY TO THE CENTRE OF AXILLARY SPECIMENS FROM HIDRADENITIS PATIENTS

* FIBROSIS PRESENT

FIGURES IN PARENTHESES REPRESENT MEAN VALUES FOR THAT RING (T.S.A. ÷ 8)
T.S.A. = TOTAL SURFACE AREA

SEX	T.S.A. PERIPHERY	T.S.A. 1 CM. FROM PERIPHERY	T.S.A. 2 CM. FROM PERIPHERY	T.S.A. 3 CM. FROM PERIPHERY	T.S.A. 4 CM. FROM PERIPHERY	T.S.A. CENTRAL SAMPLE
FEMALE	5.2 (0.65)	30.9 (3.9)	261 (32.6)	-	-	49.5
FEMALE	0	10.4 (1.3)	83.2 (10.4)	-	-	28.9
FEMALE	0.5 (0.06)	6.3 (0.79)	111.6 (13.9)	-	-	16.9
FEMALE	2.1 (0.26)	51.7 (6.5)	138.8 (17.3)	-	-	17.5
FEMALE	24.4 (3.04)	30.9 (3.9)	-	-	-	13.6
FEMALE	17.7 (2.2)	15.4 (1.9)	76.7 (9.6)	-	-	14.3
FEMALE*	2.8 (0.34)	3.5 (0.4)	58.4 (7.3)	-	-	2.9
FEMALE	0	120.4 (15)	155.0 (19.4)	-	-	46.6
FEMALE	6.8 (0.9)	15.2 (1.9)	99.8 (12.5)	-	-	20.9
FEMALE	31.4 (3.9)	109.4 (13.7)	208.8 (26.1)	-	-	26.3
MALE*	0	9.85 (1.23)	47.5 (5.9)	135.8 (16.9)	-	4.7
MALE	19.1 (2.4)	53.7 (6.7)	98.1 (12.3)	-	-	20.9

The total surface area of the apocrine tubules increased as one moved from the periphery to the centre of the axilla. In the 10 hidradenitis patients without fibrosis there was a progressive gradient towards the centre with a probability of 6.3×10^{-14}. The 2 patients with fibrosis showed a clearly different pattern, with a low apocrine tubule surface area in the centre. The hypothesis that there is a gradient away from the centre is equally geometrically plausible, but for whichever model is fitted, the 10 hidradenitis patients can always be assigned a probability of at least 0.002.

It can also be seen, that in all but 3 of the 12 hidradenitis patients, some apocrine sweat tissue was still present at the periphery of the excised skin, despite the pre-operative use of the atropine/iodine/starch and oxytocin method.

The distribution of the apocrine glands in the axilla as revealed by microscopy corresponded with that revealed by the atropine/iodine/starch and oxytocin method.

7.1.3 MICROSCOPIC STUDY OF WIDELY EXCISED CADAVERIC AXILLARY SPECIMENS

The results are shown in Table 12b. The 3 normal cadaveric specimens showed the same pattern as the living hidradenitis patients i.e. an increasing apocrine gland surface area from the periphery to the centre with a probability of 0.000014.

7.2 THE DISTRIBUTION OF THE APOCRINE GLANDS IN THE PUBO-INGUINO-PERINEAL REGION

7.2.1 The results are shown in Table 13. Apocrine glands were found in 55%, 18% and 17% of the peripheral blocks of 3 of the female patients. No apocrine glands were found at the periphery in one male and one female patient. When the positive apocrine blocks were related by photography to their original situation in the patient, they were found to be concentrated in the external aspects of the labia majora, and extending into the adjacent mons

TABLE 12b. SURFACE AREA OF APOCRINE TUBULES, FROM THE PERIPHERY TO THE CENTRE OF AXILLARY SPECIMENS FROM CADAVERS

FIGURES IN PARENTHESES REPRESENT MEAN VALUES FOR THAT RING (T.S.A. ÷ 8)

T.S.A. = TOTAL SURFACE AREA

SEX	T.S.A. PERIPHERY	T.S.A. 1 CM. FROM PERIPHERY	T.S.A. 2 CM. FROM PERIPHERY	T.S.A. 3 CM. FROM PERIPHERY	T.S.A. 4 CM. FROM PERIPHERY	T.S.A. CENTRAL SAMPLE
MALE CADAVER	0	0	8.7 (1.09)	-	36 (4.5)	25.5
MALE CADAVER	0	0	6.3 (0.79)	18.06 (2.26)	42.8 (5.3)	63.1
FEMALE CADAVER	0	0	0	11.97 (1.49)	17.9 (2.25)	9.4

TABLE 13. MICROSCOPIC EXAMINATION OF BLOCKS OBTAINED FROM THE PERIPHERY OF PUBO-INGUINO-PERINEAL SPECIMENS.

SEX	NUMBER OF BLOCKS	NUMBER OF BLOCKS POSITIVE FOR GLANDS	SITUATION OF APOCRINE GLANDS
MALE	18	0	-
FEMALE	21	0	-
FEMALE	20	11 (55%)	MONS PUBIS, LABIA MAJORA, MEDIAL GROIN, PERIANAL AREA.
FEMALE	22	4 (18%)	MONS PUBIS, LABIA MAJORA, MEDIAL GROIN, PERIANAL AREA.
FEMALE	18	3 (17%)	MONS PUBIS, LABIA MAJORA, MEDIAL GROIN, PERIANAL AREA.

pubis, medial aspects of the groin and upper thigh and extending into the skin of the perianal area.

7.2.2 The distribution of the apocrine glands as determined by the examination of multiple blocks taken throughout the radically excised hidradenitis specimens is shown in Table 14. Apocrine glands were found in 24%, 20%, 13%, 33%, 23%, 14% and 13% of the blocks from the 7 patients. In the females, the most consistent site at which apocrine glands were found, was the external aspects of the labia majora, which were included in the operative specimen. The apocrine glands extended to a variable degree into the adjoining medial groin plus upper thigh, the skin of the mons pubis and into the perineal skin. The inner aspects of the labia majora and the labia minora were not excised at operation and it is, therefore, impossible to comment upon the presence or absence of apocrine glands in these areas.

In the male, the apocrine glands were situated, again to variable extent, at the junction of the medial groins and upper thigh with the scrotal skin, extending down to the perineal area and around the root of the penis and the adjacent pubic skin.

In both males and females, the apocrine glands were smaller than in the axilla, but the most marked difference was related to confluence of the glands. The apocrine glands in the axilla were near confluent, those in the pubo-inguino-perineal area were isolated, scattered and small in number. Nearly all the blocks in the pubo-inguino-perineal area showed the presence of eccrine glands and pilo-sebaceous units, whereas the apocrine sweat glands were only occasionally seen.

7.2.3 The results are shown in Table 15. Apocrine glands were found in 100%, 10% and 9% of the blocks taken from wide excisions of the groin.

TABLE 14. MICROSCOPIC EXAMINATION OF PUBO-INGUINO-PERINEAL SPECIMENS AFTER COMPLETE BLOCKING.

SEX	NUMBER OF BLOCKS	NUMBER OF BLOCKS POSITIVE FOR GLANDS	SITUATION OF APOCRINE GLANDS
FEMALE	71	17(24%)	LABIA MAJORA, GROIN, PUBIS, PERIANAL SKIN.
FEMALE	85	17(20%)	LABIA MAJORA, PUBIS.
FEMALE	75	10(13%)	LABIA MAJORA, GROIN, PUBIS.
FEMALE	72	9(13%)	LABIA MAJORA, GROIN, PUBIS, PERIANAL SKIN.
MALE	120	27(23%)	GROIN, UPPER THIGH, PERIANAL SKIN.
MALE	66	9(14%)	ROOT OF PENIS, PUBIS, GROIN, SCROTUM.
MALE	99	33(33%)	GROIN, THIGH, SCROTUM, ROOT OF PENIS, PUBIS.

TABLE 15. MICROSCOPIC EXAMINATION OF SKIN OBTAINED AT LOCAL EXCISION OF THE GROIN, FOR THE PRESENCE OF APOCRINE GLANDS.

SEX	NUMBER OF BLOCKS TAKEN	NUMBER OF BLOCKS POSITIVE FOR GLANDS
FEMALE	5	5(100%)
FEMALE	10	1 (10%)
FEMALE	11	1 (9%)

DISCUSSION

7.1 (1+2) MICROSCOPIC STUDY OF RADICALLY EXCISED AXILLARY SPECIMENS

Analysis of the results obtained shows that the greater the extent of the axillary excision performed, the greater the chance of completely clearing the apocrine gland containing skin in this area. The histological study of the surface area of the apocrine tubules along the 8 radii at one centimetre intervals, also shows that there is an increasing concentration of apocrine glands from the periphery towards the centre of the axilla.

Examination of the photographs obtained of axillae undergoing the atropine/iodine/starch and oxytocin test, Figs. 14 and 15, show a similar distribution of apocrine sweat. The droplets being particularly dense at the centre of the hair growing area and becoming less frequent as the periphery is reached but some droplets being present outside the hairy area.

Because of the thinly scattered distribution of apocrine glands outside the hair growing area, isolated apocrine glands could be found at the periphery of the excised axillary specimens, whether or not the atropine/iodine/starch and oxytocin method was used. This probably explains the one recurrence experienced following axillary excision (Chapter IX), where the male patient concerned had isolated apocrine sweat glands extending in a scattered fashion from the axilla over the chest wall.

7.1.3 MICROSCOPIC STUDY OF WIDELY EXCISED CADAVERIC SPECIMENS

The distribution of the apocrine sweat glands in the axillary skin of normal cadaveric specimens was the same as in hidradenitis. Much wider excisions had been performed on the cadavers and there were no apocrine glands found at the margins of excision. This may suggest that wider excisions than we performed in hidradenitis patients could clear all the apocrine glands, or that the lack of apocrine glands at the margins of the cadaveric specimens was fortuitous or alternatively that ectopic apocrine glands may involute in old age (the age of the cadavers ranged from 74 to 85 years at the time of their death).

7.2 THE DISTRIBUTION OF THE APOCRINE GLANDS IN THE PUBO-INGUINO-PERINEAL REGION

The apocrine glands in the pubo-inguino-perineal region were much smaller and much fewer than in the axilla. It would appear unlikely, that the explanation for this, would be their destruction by the disease process, as this also pertained to non-diseased areas of skin and, also, that the eccrine and sebaceous glands were intact in the diseased areas.

The distribution of the apocrine glands in this region, correlated with the distribution as demonstrated by the atropine/iodine/starch and oxytocin method.

CHAPTER VIII

MICROSCOPIC FEATURES OF HIDRADENITIS

IN RELATION TO THE APOCRINE GLANDS

CONTENTS PAGE

MICROSCOPIC FEATURES OF HIDRADENITIS IN RELATION TO THE APOCRINE GLANDS

INTRODUCTION

Microscopic studies of diseased skin in hidradenitis have led to opinions as opposite as that the inflammatory process commences in the apocrine glands (Brunsting 1939), to that of Anderson and Dockerty (1958) who considered that the apocrine glands were not of primary importance.

This chapter describes a microscopic study of areas of skin macroscopically involved by hidradenitis, with particular attention to the anatomical relationship between the inflammatory process and the apocrine glands.

PATIENTS AND METHODS

8.1 MICROSCOPIC STUDY OF AREAS OF SKIN SHOWING THE MACROSCOPIC CHANGES OF HIDRADENITIS

One cm^2. samples of skin, including the underlying subcutaneous tissue, were excised from the visibly diseased areas of the operative specimens. These specimens were obtained from:- the axillae in 29 cases, the groins in 12, the perineal area in 10, the pubic area in 9, the perianal area in 5, the skin overlying the sternum in 4, the infra-mammary folds of the breasts in 2, and the nape of the neck in one. Five sections were cut through each sample, in a plane vertical to the skin surface. The sections were stained with H. & E. and examined under a light microscope.

The 5 patients with perianal disease had undergone a wide excision of the perianal skin, leaving a narrow margin around the anus. While blind sinus formation was not uncommon, fistula in ano was not seen. The wounds were allowed to heal by granulation with Silastic Foam dressing, without a diverting colostomy.

RESULTS

8.1 THE MICROSCOPIC STUDY OF AREAS OF SKIN SHOWING THE MACROSCOPIC CHANGES OF HIDRADENITIS

The diseased skin of the axilla showed a convoluted surface, with deep irregular sinuses, either lined by inflammatory granulation tissue or epithelium. Hair follicles were present, sometimes showing keratinous plugging of their orifices. Fibres of the erector pilorum muscles were visible, as were sebaceous glands adjacent to the hair follicles. Fibrosis of the dermis and subcutaneous tissue varied considerably; at its maximum, there was a complete lack of glandular structures. More often, apocrine and eccrine sweat glands could be visualised; the presence of apocrine glands being more variable. A mild to dense inflammatory infiltrate was present. The majority of the cells, being lymphocytes but plasma and foreign body giant cells could be visualised. The inflammatory reaction was often so extensive that it was impossible to recognise any skin structures. Where it was possible to visualise these structures amongst the inflammatory infiltrate, it was not possible to relate the inflammatory cells to any one particular skin structure. Inflammatory cells were as common around eccrine sweat glands as around apocrine glands. The inflammatory cells were never confined to the lumens of the apocrine glands and they appeared to be distributed throughout the dermis, exterior to the sweat glands, Figs. 22, 23 and 24.

The findings were similar in the skin of the groins, pubic and perineal areas. The major difference in these areas to the axilla, was the comparative lack of apocrine sweat glands. Apocrine glands were uncommon in healthy areas of skin taken from this region, but were rare in the diseased area. However, eccrine sweat and sebaceous glands were always to be seen amongst the inflammatory cells.

Large apocrine glands were seen in the perianal skin. Otherwise the inflammatory infiltrate, fibrosis and sinus formation was similar to that outlined above.

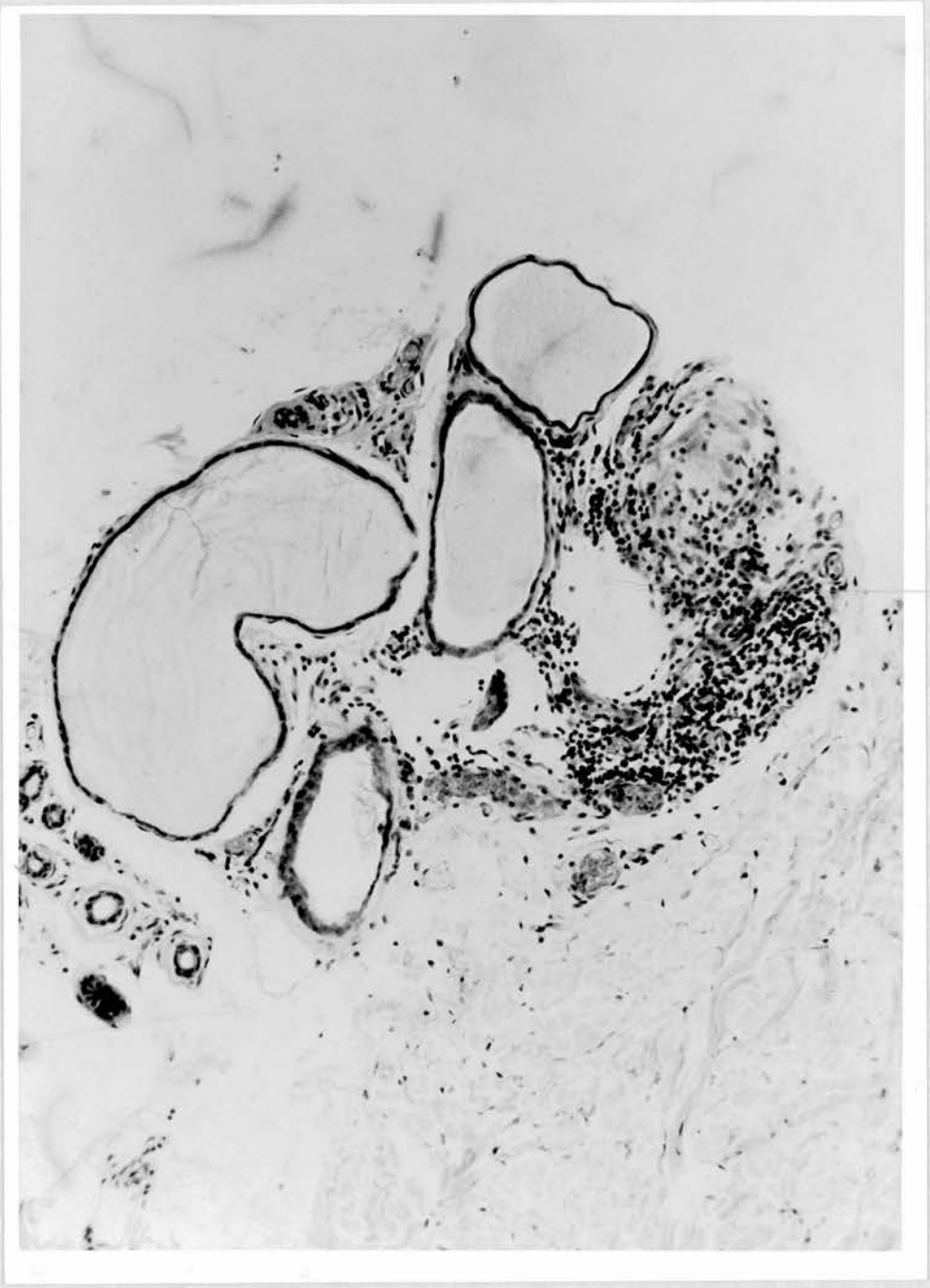


FIG. 22. 'CYSTIC' DILATATION OF APOCRINE GLANDS. INFLAMMATORY CELLS RELATED TO HAIR FOLLICLE.

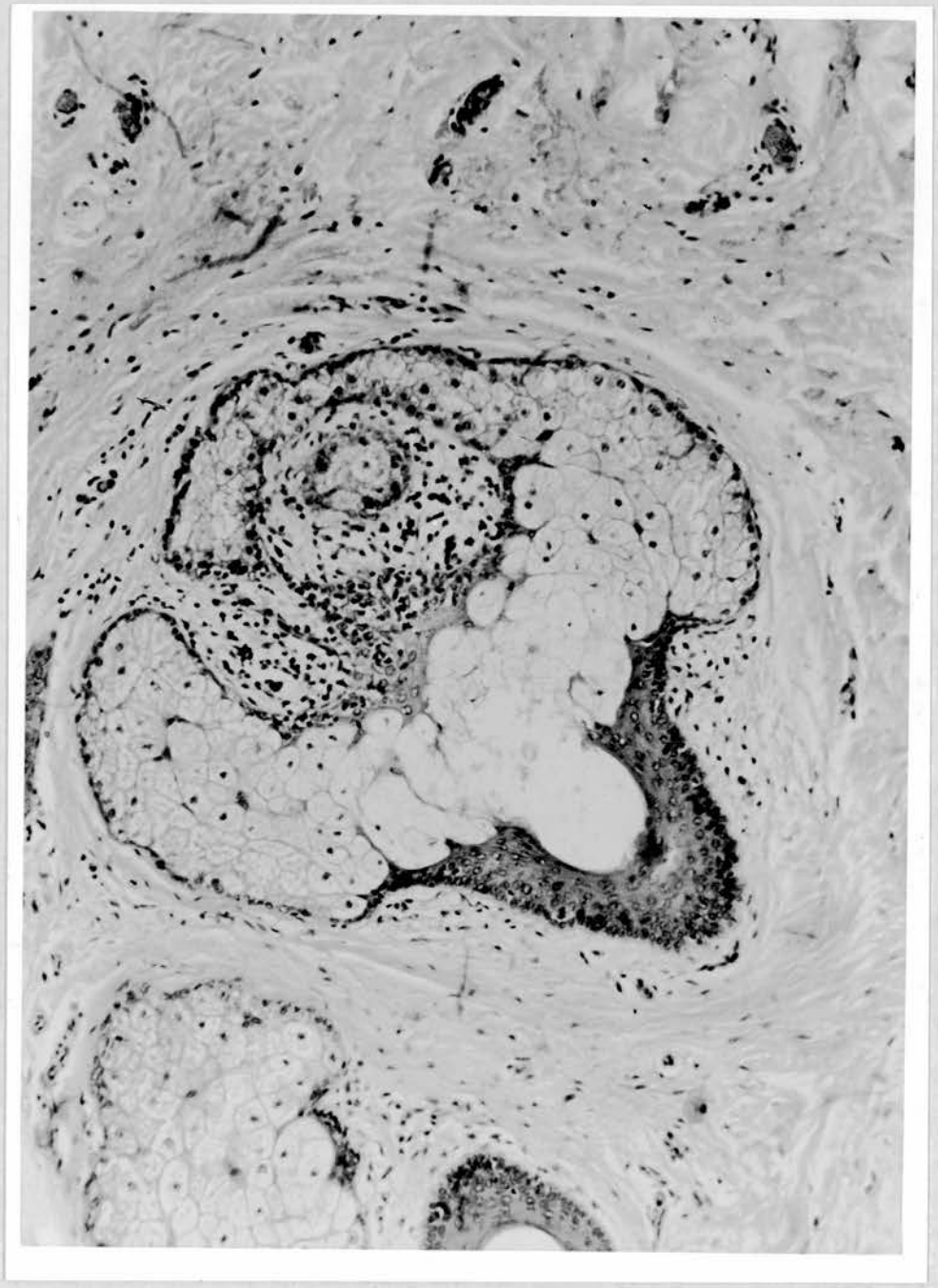


FIG. 23. INFLAMMATORY CELLS RELATED TO HAIR FOLLICLE AND SEBACEOUS GLANDS IN HIDRADENITIS.

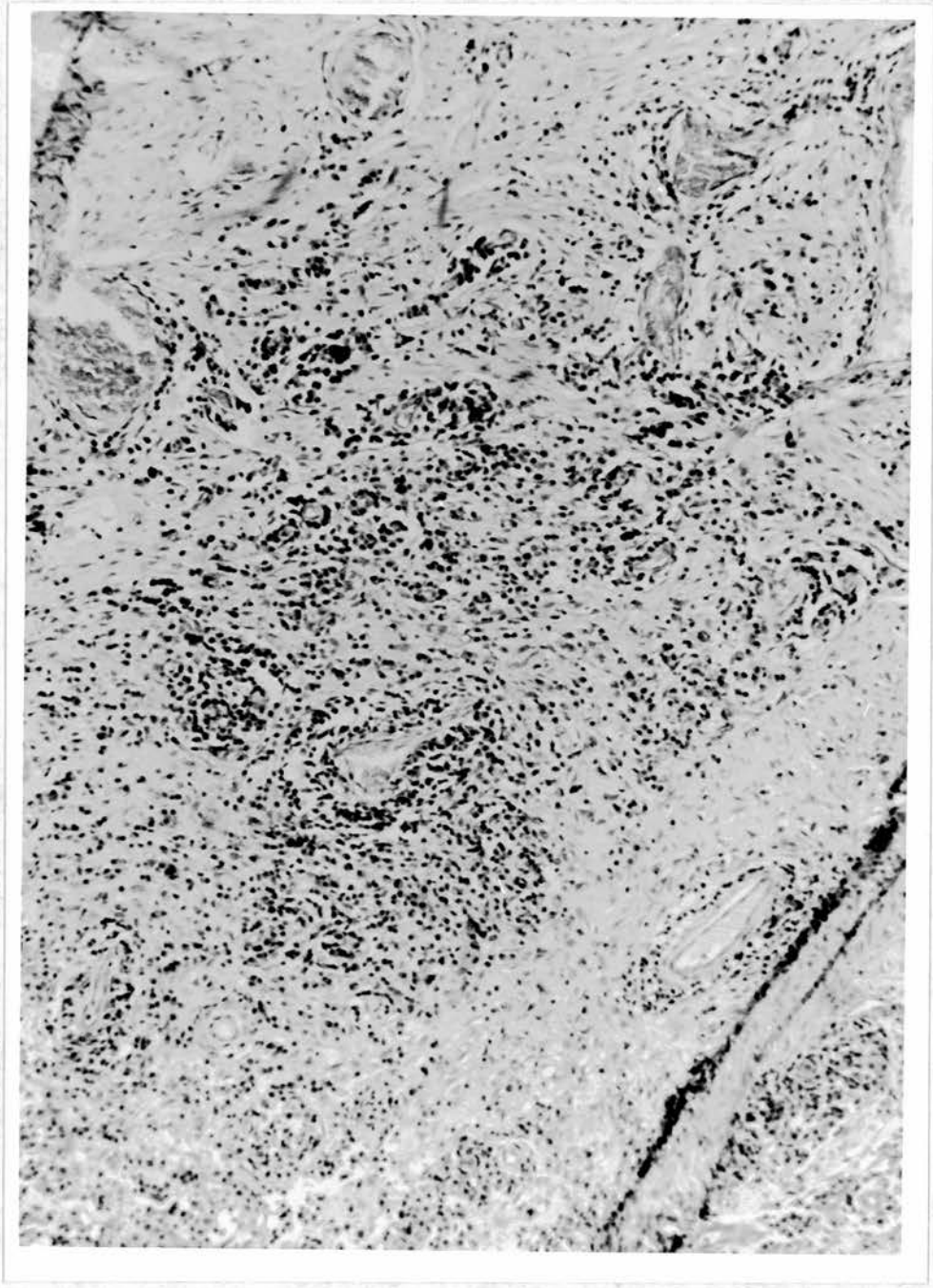


FIG. 24. DIFFUSE CHRONIC INFLAMMATORY REACTION IN HIDRADENITIS.

Microscopic examination of the skin taken from the back of the neck, over the sternum and from the inframammary areas showed the same inflammatory cell infiltrate and sinus formation. However, apocrine sweat glands were never seen, although eccrine glands were always present.

There was no instance of malignant change, in particular, squamous cell carcinoma, in any of the blocks of skin examined during this series.

DISCUSSION

8.1 THE MICROSCOPIC STUDY OF AREAS OF SKIN SHOWING THE MACROSCOPIC CHANGES OF HIDRADENITIS

The localisation of hidradenitis in its most classical form to areas of the body e.g. the axillae or groins, that possess the distinction of having concentrations of apocrine glands, led to the association of hidradenitis with these glands. Brunsting (1939) considered that the inflammatory process commenced in the apocrine glands, and then spread through the subcutis by means of the lymph channels. Anderson and Dockerty (1958) felt that the paucity of apocrine glands in sections of skin, taken from the pubo-inguino-perineal region of hidradenitis patients, compared to the abundance of eccrine and sebaceous glands, could not be explained by the disease process. They also noted that peri-glandular inflammation was common about apocrine, eccrine, sebaceous glands and hair follicles, to an equal extent. In no section, was evidence of inflammation found within the coil of a sweat gland, either apocrine or eccrine; on the contrary, inflammatory cells could be seen in the periglandular tissues, while the lumens and cells of those glands were uninvolved. They concluded that the apocrine glands were not of primary importance in hidradenitis.

The findings in this series were very similar to those of Anderson and Dockerty (1958). While apocrine glands were plentiful in axillary specimens, they were scarce in skin taken from the groins, even when minimally involved skin was microscopically examined. In areas such as the nape of the neck, skin over the sternum and inframammary folds; where the macroscopic appearance of the disease was that of hidradenitis; no apocrine glands could be visualised on microscopic examination. The periumbilical area contains apocrine glands and yet hidradenitis is rarely seen at this site.

In addition, the chronic inflammatory cells were mainly situated in the periglandular tissues, and were never seen to be confined to the apocrine sweat glands.

While this does not prove that apocrine glands are not primarily involved in hidradenitis, it certainly does not help to confirm

the hypothesis. Good evidence of the primary involvement of the apocrine sweat glands in the pathogenesis of hidradenitis has yet to be produced. The distribution of the disease could be explained on the basis of follicular occlusion by hyperkeratosis, occurring in areas where the skin is moist and recessed, and supporting a suitable bacterial flora.

Malignant change in hidradenitis occurs in the pubo-inguino-perineal region, after many years of involvement. It was not seen in this series, presumably because the patients presented for definitive management at a sufficiently early stage in the disease process.

SECTION D

THE SURGICAL TREATMENT

OF HIDRADENITIS

CHAPTER IX

RADICAL EXCISION OF APOCRINE GLAND CONTAINING SKIN IN DISEASED AREAS

CONTENTS PAGE

INTRODUCTION

The past experience in our unit has led to the conclusion that local excisions of hidradenitis result in an unacceptably high rate of recurrence of the disease. The aim of this study was to assess the effectiveness of radical excision of the apocrine gland containing skin in the diseased region in curing hidradenitis. The success of this method of treatment to be assessed by the recurrence rate at follow up. The two areas studied were the axilla and the pubo-inguino-perineal region.

PATIENTS AND METHODS

9.1 RADICAL EXCISION OF THE AXILLARY SKIN

Forty-two (42) patients, comprising 33 females and 9 males underwent radical excision of the axillary skin. Thirty-one (31) patients, had both axillae excised at the same operation. Nine (9) patients had only one axilla excised. Two (2) patients had both axillae excised but metachronously. A total of 75 excisions of axillary skin were, therefore, carried out in the 42 patients. All the patients had chronic hidradenitis suppurativa, with bands of fibrosis and discharging sinuses in the axilla. The extent and protraction of the disease severely affecting the patients' quality of life.

The extent of the excisions were based on the iodine/starch/oxytocin test (Chapter VI) or prior to its use on the knowledge that the apocrine ducts open mainly into hair follicles and that, therefore, the apocrine glands would be concentrated in the hair growing area of the axilla. Both methods resulted in excisions of similar extent and configuration, Fig. 25.

The hair growing area of the axillary skin was excised together with a surrounding one centimetre margin of normal skin. As the apocrine glands can extend into the subcutaneous fat, the excisions included 0.5 cm. of fat. In some of the patients, deep burrowing sinuses extended down as far as the axillary fascia, and in order to avoid lymphatic damage, that may have resulted from deep excisions, the sinuses were laid open and curetted. Haemostasis was secured and the wound dressed with a gauze roll soaked in acriflavine/paraffin emulsion, Fig. 26.

When a skin graft was to be used to repair the axillary defect, a thin split skin graft was taken at the primary operation, from high on the inner aspect of the thigh. The graft was stored in a sterile saline filled container, at $4^{\circ}C.$, until used for delayed grafting.

FIG. 25. AXILLA MARKED OUT FOR EXCISION.

FIG. 26. EXCISED AXILLA.

9.2 RADICAL EXCISION OF THE PUBO-INGUINO-PERINEAL SKIN

Twenty-one (21) patients, 14 females and 7 males, with chronic hidradenitis underwent radical excision of the pubo-inguino-perineal region.

Pubo-inguino-perineal disease, both in the male and female, occurred mainly in the medial halves of the groins, with involvement of the external aspects of the labia majora in the female and the adjacent one centimetre or so of scrotal skin in the male. The skin over the mons pubis and the perineal skin were variably involved.

Based on the distribution of the apocrine glands as demonstrated by the iodine/starch/oxytocin method, the extent of the excision was designed to include, as far as was practical, all the apocrine gland containing skin in this region. In the female, the skin excised comprised that over the mons pubis, extending laterally to meet the inguinal ligaments and taking the medial halves of the groins and adjacent thigh skin with 2 cm. of normal clearance, and medially removing the outer aspects, only, of the labia majora. The skin excised broadened lateral to the perianal area, to clear any overt disease by 2 cm. A narrow strip of skin was preserved in the midline, between the anus and the vagina. Care was taken to preserve a rim of skin at the base of the mons pubis around the clitoris, and to preserve the skin of the inner aspects of the labia majora and of the perineal raphe. Fig. 27 demonstrates the extent of the excision.

The extent of the excision was similar in the male. Any scrotal disease adjacent to the groin was cleared by a one centimetre strip of normal scrotal skin. See Fig. 28 for the extent of the excision in the male.

Perianal hidradenitis was uncommon in this series. When it occurred, it was not considered practicable to perform an excision of that area in continuity with the radical pubo-inguino-perineal dissection. When necessary, excision of the perianal skin was carried out

FIG. 27. FEMALE PUBO-INGUINO-PERINEAL AREA MARKED OUT FOR RADICAL EXCISION.

FIG. 28. RADICALLY EXCISED MALE PUBO-INGUINO-PERINEAL AREA.

as a secondary procedure.

The pubo-inguino-perineal dissection was performed with the patient supine. The legs and abdomen were prepared with antiseptics and the legs towelled with sterile tubular bandage (Tubigrip), in order to facilitate their movement during the posterior perineal part of the dissection. The depth of excision did not exceed 0.5. cm. in order to avoid interference with the lymphatics. Care was taken to avoid deep excision particularly in the region of the root of the penis and mons pubis, in order to minimise post-operative preputial or labial oedema. Deep excisions of the labia majora are both unnecessary and can lead to troublesome bleeding. Haemostasis having been obtained a urinary catheter was inserted, and the wound packed with gauze, well soaked with acriflavine/paraffin emulsion. On the second or third post-operative day, the dressing was removed in the operating theatre under a general anaesthetic and was replaced by the first Silastic dressing.

POST-OPERATIVE FOLLOW UP

Full healing having occurred, the patients were seen at 3 monthly intervals, in order to assess the recurrence rate.

RESULTS

9.1 RADICAL EXCISION OF THE AXILLARY SKIN

Seventy-five radical excisions of axillary skin were performed in 42 patients (33 females and 9 males). The mean diameters of the excised skin specimens were 10 x 8 cm., when the 2 maximum diameters were measured at right angles to one another through the centre of the specimen, Table 16. The follow up of these patients has ranged from 15 to 65 months (median 39; mean 41 $\pm$ 13). In that time, one male patient who had a bilateral radical axillary dissection has developed recurrent hidradenitis at the periphery of the right axilla over the anterior axillary fold. When that axilla was re-examined using the iodine/starch/oxytocin method, droplets were obtained extending in a thinly scattered fashion from the axilla to the anterior chest wall. A further excision was performed, with no further recurrence to date. There have been no recurrences in the remainder of the patients. Two female patients who had undergone successful unilateral axillary excision, developed hidradenitis in the previously unaffected axillae, and had these excised.

9.2 RADICAL EXCISION OF THE PUBO-INGUINO-PERINEAL SKIN

Twenty-one patients (14 females and 7 males) underwent radical excision of the pubo-inguino-perineal region. The post-operative follow up of these patients has ranged from 23 to 96 months, with a median follow up period of 43 months (mean 47 months), Table 17.

In that time 5 patients (23.8%) have developed a local recurrence of hidradenitis adjacent to the scar in the skin of the lower abdomen, thigh or inner aspect of the labium majus. In all cases, these lesions have been solitary and effectively managed by local excision.

One of the female patients was particularly interesting. Prior to operation, she had regularly experienced an exacerbation of her pubo-inguino-perineal hidradenitis, in association with her menstrual periods. Following surgery, there was no recurrence

TABLE 16. RESULTS OF RADICAL EXCISION OF THE AXILLAE FOR HIDRADENITIS

SEX	SIDE	FOLLOW UP MONTHS	RECURRENCE
FEMALE	R + L	39	-
FEMALE	R + L	36	-
FEMALE	R + L	38	-
FEMALE	R + L	62	-
FEMALE	R + L	36	-
FEMALE	R + L	48	-
FEMALE	R + L	36	-
FEMALE	R + L	31	-
FEMALE	R + L	28	-
FEMALE	R + L	24	-
FEMALE	R + L	24	-
FEMALE	R + L	27	-
FEMALE	R + L	35	-
FEMALE	R + L	40	-
FEMALE	R + L	38	-
FEMALE	R + L	24	-
FEMALE	L	65	-
	R	24	-
FEMALE	R	38	-
FEMALE	L	60	-
FEMALE	R	39	-
	L	15	-
FEMALE	L	41	-
FEMALE	R	24	-
FEMALE	R	31	-
FEMALE	L	46	-
FEMALE	R	15	-

TABLE 16, continued.

SEX	SIDE	FOLLOW UP MONTHS	RECURRENCE
FEMALE	R	31	-
FEMALE	R + L	46	-
FEMALE	R + L	49	-
FEMALE	R + L	53	-
FEMALE	R + L	55	-
FEMALE	R + L	48	-
FEMALE	R + L	57	-
FEMALE	R + L	51	-
MALE	R + L	60	-
MALE	R + L	39	-
MALE	R + L	55	-
MALE	R + L	27	-
MALE	R + L	48	RECURRENCE
MALE	R + L	54	-
MALE	R + L	56	-
MALE	R + L	58	-
MALE	R	41	-

TABLE 17.

RADICAL EXCISION OF PUBO-INGUINO-PERINEAL HIDRADENITIS

SEX	METHOD	TIME TO HEALING (WEEKS)	LENGTH OF FOLLOW UP (MONTHS)	COMPLICATIONS/ RECURRENCE
FEMALE	SFD	6	36	NIL
FEMALE	SFD	11	33	PAINFUL SCAR, RE-EXCISED HEALING 12 WEEKS DEVELOPED RECURRENCE
FEMALE	SFD	10	48	NIL
FEMALE	SFD	6	60	LOCAL RECURRENCE
FEMALE	SFD	9	67	NIL
FEMALE	SFD	12	23	NIL
FEMALE	SFD	9	57	ERYTHEMA WITH MENSTRUAL PERIODS
FEMALE	SFD	6	60	NIL
FEMALE	SFD	16	43	NIL
FEMALE	SFD	9	49	NIL
FEMALE	SFD	9	60	LOCAL RECURRENCE
FEMALE	SFD	9	26	NIL
FEMALE	SFD	10	39	NIL
FEMALE	SFD	9	30	NIL
MALE	SFD	10	96	LOCAL RECURRENCE
MALE	SFD	11	27	NIL
MALE	SFD	23	24	NIL
MALE	SFD	10	34	NIL
MALE	SFD	15	65	LOCAL RECURRENCE
MALE	SFD	16	43	NIL
MALE	SFD	12	84	NIL

of the lesions of hidradenitis, but again in association with her menstrual periods, the whole of her lower abdomen, thighs and perineum became suffused and erythematous, only to settle completely after cessation of the period. During these episodes she became pyrexial but urine and blood cultures were negative. Antibiotics including Metronidazole were tried on an empirical basis with no effect. She was eventually subjected to a radiation menopause, with complete disappearance of her symptoms.

DISCUSSION

9.1 RADICAL EXCISION OF THE AXILLARY SKIN

Forty-two patients underwent radical excision of the skin of 75 axillae. The mean diameters of the contracted skin specimens were 10 x 8 cm. At a medial follow up of 39 months, hidradenitis had recurred in only one axilla.

Knaysi, Cosman and Crikelair (1968) performed a total excision of the hair bearing area where generalised disease existed, but a distinction was made between disease requiring only a superficial excision and that requiring a deeper excision. At a mean follow up of 37 months (median 24 months) there had been no recurrences in the 46 axillae superficially excised, but 2 recurrences occurred in the 9 axillae deeply excised.

Pollock, Virnelli and Ryan (1972) excised all grossly visible disease in 10 consecutive patients with hidradenitis. The excisions were large in that they averaged 15 x 8 cm. in the contracted specimen. At follow up ranging from 6 weeks to 12 months (no median or mean value given) no recurrent disease had appeared.

Tasche, Angelats and Jayarm (1975) having read the above paper, altered their own technique to perform larger excisions (average size of excisions 52 cm^2.) than formerly, and obtained lower recurrence rates.

This evidence suggests that radical excision of the hair bearing area and of all grossly visible disease will cure most cases of axillary hidradenitis. The depth of excision also being important, and we would advocate that the excision should be carried down to the axillary fascia, with curettage of any deeper sinuses.

Our only recurrence had apocrine glands extending outwith the confines of the axilla. It is possible that this may relate to the development of recurrent disease. However, the finding of residual apocrine tissue at the margins of excision, following radical axillary excision (Chapter VII), without recurrence, makes this unlikely. Recurrent disease may be related to ectopically

situated hair follicles.

9.2 RADICAL EXCISION OF THE PUBO-INGUINO-PERINEAL SKIN

Our aim in the pubo-inguino-perineal region was to ascertain the effectiveness of complete excision of the apocrine glands in that region in curing hidradenitis. The atropine/iodine/starch and ocytocin method was used pre-operatively to demonstrate the distribution of the apocrine glands. This method demonstrated that it was not practicable to excise the whole of the apocrine gland containing skin, as the glands extended in a scattered solitary fashion over the abdomen. The excisions performed were wide, and removed the concentrated areas of glands which corresponded with the sites of disease presentation. Thus the skin of the groins, pubis, perineum and external aspects of the labia majora were excised in the female. The areas excised in the male were similar, but the margins of the scrotum were excised in place of the external aspects of the labia majora.

It is difficult to compare the extent of excision in our series with those of others. Newell, Voelter and Mullins (1973) and Barron (1970) de-roofed the tracks followed by curettage and electrocoagulation. There was no attempt to excise the apocrine gland containing skin in the area. Thornton and Abcarian (1978) performed wide excisions of the diseased area; the extent of excisions falling into 3 groups:- 2 x 2 cm., 2 - 5 cm. x 2 - 5 cm.; and more than 5 cm. in any dimension. The majority of excisions in the latter series would be small compared to ours, and again there was no attempt to excise all the areas where the apocrine glands were concentrated in this region. Ariyan and Krizek (1976), Vickers (1975), Jackman (1942) and others also limited their surgery to wide excisions of the diseased area. As far as can be determined from reported series, our series is the first where there has been a conscious attempt to excise the concentrated areas of apocrine glands in the pubo-inguino-perineal region.

Five of the 21 patients who underwent radical excision of the

pubo-inguino-perineal region in our series developed recurrent hidradenitis, at a median follow up of 43 months. In all cases the recurrences were solitary, small and situated at the margins of excision and were possibly due to the remaining scattered apocrine glands or hair follicles over the abdomen.

There are only 2 series reported in the literature where it is possible to make a tentative comparison with ours. Four of the 104 patients in Thornton and Abcarian (1978) series developed recurrent hidradenitis over the 5 year period of the study. This recurrence rate is low compared to ours, but many of the incisions in the latter series were small and probably performed for minimal disease. Their results, therefore, cannot be strictly compared with ours which were for generalised chronic disease. Anderson and Dockerty (1958) treated 64 patients with perineal and perianal disease, 26 of whom were lost to follow up. Of the remaining 38 patients, 79% developed recurrent hidradenitis. The latter recurrence rate is much higher than ours, but it is not clear from their report as to the size of excisions performed or as to the proportions of perineal and perianal disease treated.

Our method of radical excision of the pubo-inguino-perineal region is effective in curing the majority of patients with hidradenitis in this region. However, a low recurrence rate is to be expected.

CHAPTER X

METHODS OF OBTAINING HEALING

FOLLOWING RADICAL EXCISION

CONTENTS PAGE

INTRODUCTION

Wide excision of the apocrine gland containing skin in hidradenitis results in large cutaneous defects. This chapter describes a study comparing healing by granulation versus split skin grafting in the healing of the axillary defects; and examines healing by granulation in the pubo-inguino-perineal region.

These methods were assessed in terms of rate of healing, limb mobility and contracture formation.

PATIENTS AND METHODS

10.1 A COMPARISON OF SKIN GRAFTING VERSUS HEALING BY GRANULATION, FOLLOWING AXILLARY EXCISION FOR HIDRADENITIS

Ten (10) patients (7 females and 3 males), undergoing bilateral radical excision of the axillary skin were studied. Prior to surgery, each axilla was assigned alternately, for successive patients to grafting or healing by granulation. Thus each patient received a split skin graft to one axilla; the opposite axilla healing by granulation, and acted as their own control. The axillary apocrine glands were defined by the iodine/starch/oxytocin method and this area was then excised, as described above.

Following excision, acriflavine and paraffin soaked packs were applied to both axillae, and a split skin graft obtained. At 48 hours, the packs were removed and Silastic dressing (Dow Corning) applied to one axilla and the graft to the other. Using a sterile technique, the grafts were removed from their container and laid on the axillary granulations, deep surface down. The graft was spread over the raw area, without wrinkles, so that exact apposition pertained; the edges of the graft overlapping the surrounding skin by 1 - 2 mms. Small fenestrations were made in the graft with scissors, in order to facilitate the drainage of serum from the axillary surface. A bulky window dressing of gauze was then placed about the site. No sutures were used to secure the graft. The ipsilateral arm was immobilised in an aeroplane splint, until the graft was firmly attached. The grafts were regularly inspected and any blebs of serum that developed under the graft were aspirated with a needle and syringe, as vascularisation of the graft would otherwise have been hindered.

Silastic Foam dressing was produced by mixing the base with a catalyst, in the proportions of 10 mls. of elastomer to 0.6 ml. of catalyst. The base and catalyst were drawn up in separate syringes and mixed in a small container with a wooden spatula for approximately 15 seconds to provide an uniform consistency. With the patient lying supine the arm on the side to be treated

was abducted and externally rotated, the hand being placed behind the head. A stiff piece of paper was held at the inferior margin of the axillary excision, and the now polymerized elastomer poured into the cavity. The Silastic dressing then expanded to four times its own volume, filling the wound and setting to a soft foam in approximately 3 minutes. The Silastic dressing was held in place by adhesive tape and the patient allowed unrestricted use of the arm, Fig. 29. The patient was instructed to remove the foam dressing twice daily and to bathe the area; the stent was washed under cold running water and soaked for 10 minutes in aqueous hibitane 1/200 solution, in order to retain its pliancy. Attention was paid to the prevention of wound bridging and the formation of excessive or unhealthy granulations.

10.2 HEALING BY GRANULATION IN THE PUBO-INGUINO-PERINEAL REGION

As in the axilla, the Silastic Foam dressing base was mixed with the catalyst in the proportion of 100 parts of base to 6 parts of catalyst. However, larger proportions were required in the pubo-inguinal region and a large wound could require 2 pourings of 20 mls. of base and 1.2 ml. of catalyst. The Silastic dressing was poured from below upwards. The 2 sides usually required a separate pouring, but the material bonded together satisfactorily. Setting occurred in approximately 3 minutes, resulting in a dressing of one centimetre in thickness. The first dressing was poured with the legs slightly abducted, to give a suitable configuration for lying in bed, but when the second dressing was poured, a few days later, the legs were adducted, as the material set, to give a suitable shape for walking, Fig. 30. Once set, the dressing could be removed and replaced with ease, without causing discomfort. The urinary catheter was removed, as soon as the patient was mobile. Micropore tape, tight underclothes, or an Elastonet body stocking were used to hold the dressing in place. The patients took a salt bath twice daily, washing the dressing in aqueous hibitane and then replacing it.

FIG. 29. SILASTIC FOAM DRESSING IN THE AXILLA.

FIG. 30. SILASTIC FOAM DRESSING IN THE PUBO-INGUINO-PERINEAL AREA.

POST-OPERATIVE FOLLOW UP

After discharge from hospital, all the patients were reviewed weekly until complete epithelialisation had taken place. The patients were then seen monthly to confirm that full limb mobility was achieved.

Full epithelial cover of the wound having been obtained, note was made of any contracture of the scar. Upper limb mobility was assessed in terms of attaining 180° of abduction at the shoulder joint and lower limb mobility by the range of abduction and external rotation at the hip joint. Upper and lower limb swelling were assessed by measuring the circumference of the upper arm, forearm and thigh at fixed points and comparing the measurements obtained with the pre-operative values at those fixed points. The fixed points were midway between the tip of the acromion and medial epicondyle of the humerus in the case of the upper arm; midway between the lateral epicondyle of the humerus and the radial styloid for the forearm; and midway between the anterior superior iliac spine and the superior border of the patella, with the patient lying supine and the legs approximated, in the case of the thigh. These details were recorded on each patient's proforma sheet at the time of their attendance.

In the case of the skin graft/healing by granulation, axillary trial, the patient preference with regard to the method of healing used, was recorded once full healing had occurred.

RESULTS

10.1 A COMPARISON OF SKIN GRAFTING VERSUS HEALING BY GRANULATION, FOLLOWING AXILLARY EXCISION FOR HIDRADENITIS

Ten patients and therefore 20 axillae have undergone a median follow up of 53.5 months (mean 52.5, range 46 - 58 months) following bilateral axillary excision. None of these patients have developed significant arm swelling, limitation of abduction or contracture formation. Table 18; Fig. 31 and Fig. 32.

The mean maximum diameters of the excised axillary skin when measured at 90° to each other, were similar for both groups; 11 x 8 cm. for the skin grafted axillae and 10 x 8 cm. for axillae receiving Silastic dressing.

The median time to complete healing was 7 weeks (mean 9; range 5 - 24) for all the grafted axillae and 12 weeks (mean 14; range 5 - 36) for all the Silastic dressed axillae. For the purpose of this study, a successful graft was defined as a greater than 50% take of the applied skin. Six of the 10 patients had a successful take (mean take 75%) using this definition, with a median and mean healing time of 6 weeks. Silastic dressings were applied to these axillae, while the areas of graft loss epithelialised. The 4 failed grafts (mean take 30%) completed healing by secondary intention, utilising Silastic dressing in 3 and Melolin dressing in one, with a median healing time of 11 weeks (mean 13 weeks).

Seven of the 10 axillae that received Silastic dressing had uneventful healing (median and mean healing times 8 and 9 weeks respectively). Of the remaining 3, one found the dressing uncomfortable (this was the same patient that found Silastic dressing uncomfortable after the skin graft failure, and used Melolin) and Melolin dressings were applied. Granulation tissue formation in the other 2 was poor and epithelialisation slow. Median and mean times to healing in this group were 24 and 27 weeks respectively.

Seven of the 10 patients, when asked to compare their grafted

TABLE 18. SKIN GRAFTING VERSUS HEALING BY GRANULATION

AFTER AXILLARY EXCISION

VALUES	SPLIT SKIN GRAFT	HEALING BY GRANULATION
SIZE OF EXCISION (CM.)	11 x 8	10 x 8
SUCCESSFUL HEALING TIMES (WEEKS)	MEDIAN 6 MEAN 6	MEDIAN 8 MEAN 9
OVERALL HEALING TIMES (WEEKS)	RANGE 5 - 24 MEDIAN 7 MEAN 9	RANGE 5 - 36 MEDIAN 12 MEAN 14

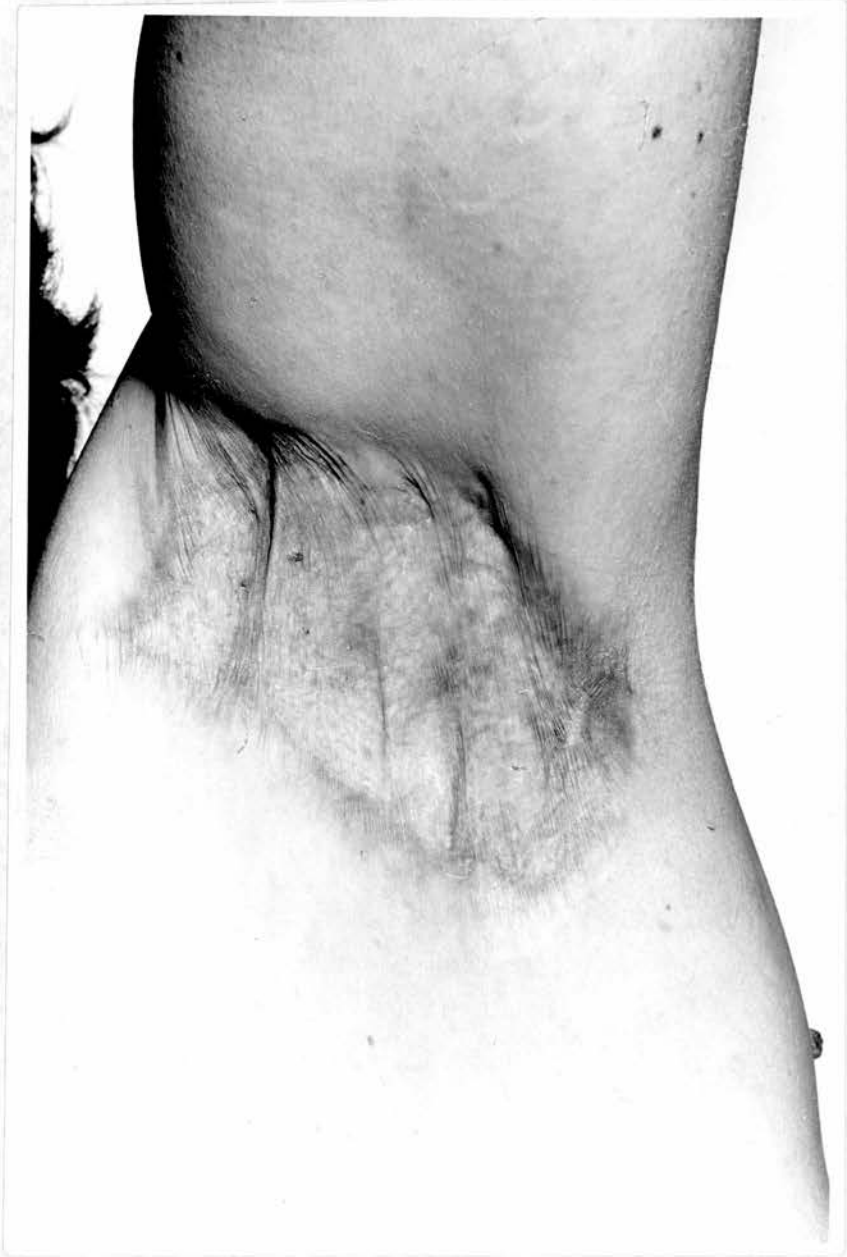


FIG. 31. HEALED GRAFTED AXILLA.

FIG. 32. AXILLA HEALED BY GRANULATION.

axilla with the opposite Silastic dressed axilla, expressed a preference for the Silastic dressing. The reasons given included its comfort, ease of use, limb freedom and lack of painful donor site. Two patients preferred the more rapid healing that they obtained with grafting and one patient disliked both methods intensely.

10.2 HEALING BY GRANULATION IN THE PUBO-INGUINO-PERINEAL REGION

Twenty-one patients (14 females and 7 males) underwent radical excision of the pubo-inguino-perineal region. In all cases healing was obtained by secondary intention with the use of Silastic dressing. The median time to healing of the resulting large defects was 10 weeks (mean 10.8; range 6 - 23 weeks). The last areas to heal following the above excisions were the posterior aspects of the perineum adjacent to the perianal area and upper thigh. Some tightness in this area was common in the early months following complete healing. However, no patient was left with limitation of bilateral hip abduction or external rotation, but many could feel a tightness in the perineum at the extremes of these movements, Table 17; Figs. 33 and 34.

Vulval oedema was common in the immediate post-operative period but this invariably settled during the ensuing 7 to 14 days, and there was no instance of narrowing of the vulval introitus.

One patient developed a painful hypertrophic scar, which persisted after healing was complete. Re-excision of the scar became necessary to obtain resolution of this problem.

The post-operative duration of hospitalisation ranged from 10 - 32 days with a median value of 14 days. Upon discharge, the patient was able to care for their own wound and dressing, with minimal support from the community nursing services.

FIG. 33. HEALED FEMALE PUBO-INGUINO-PERINEAL AREA.

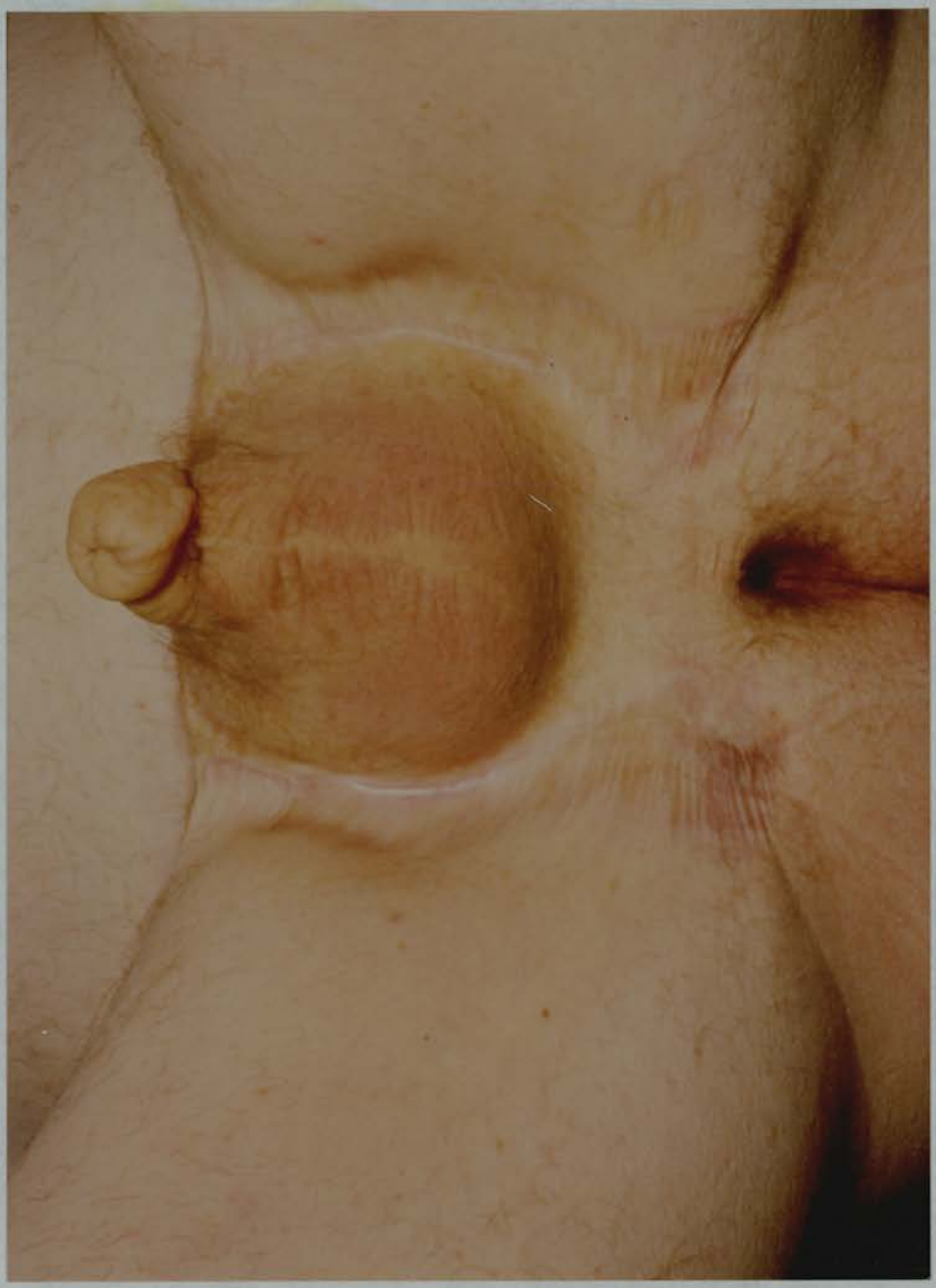


FIG. 34. HEALED MALE PUBO-INGUINO-PERINEAL AREA.

DISCUSSION

10.1 A COMPARISON OF SKIN GRAFTING VERSUS HEALING BY GRANULATION, FOLLOWING AXILLARY EXCISION FOR HIDRADENITIS

Attempts to completely excise the apocrine gland containing skin in the axilla result in large defects. A number of authors have described various methods of obtaining healing. Greely (1951) advocated immediate or delayed skin grafting, but gave no details of the numbers of patients involved or of the outcome of the treatment. Letterman and Schurter (1974) recommended primary repair of the defect using a modified Z plasty. Lipshutz (1974) advanced to the centre of the defect, 2 triangular islands constructed from the dog ears at each end of the defect. Harrison (1964) used posteriorly based transposition flaps to close the defects. Armstrong (1965) initially used split skin grafts and then later in his series, posteriorly based rotation flaps. None of these papers give any measurements of the size of excision, or of the outcome of treatment on follow up.

O'Brien, Wysocki and Anastasi (1976) advocated the use of an anteriorly based rotation flap in the female and a posteriorly based flap in the male. Details of the sizes of excision were not given, but from the photographs shown in that paper, they appeared to be small. The authors claimed good results for this technique but no details of the results were given.

It is impossible to draw any conclusions from these papers or to compare the techniques advocated with any other.

Knaysi, Cosman and Crikelair (1968) performed a total excision of the hair bearing area, where generalised disease existed. If the disease only required a superficial excision, a split skin graft was subsequently applied, but in cases requiring deeper excision, transposition flaps were used. Four of the 46 axillae that were grafted sustained graft loss (50% loss); hypertrophic scars developed in 2 instances and wound contracture in 2 instances. Transposition flaps were used in 9 axillae and were associated with the following complications:- loss of the skin graft covering

the flap donor site in 2 instances, haematoma formation in one instance, and scar contracture requiring surgical release in 2 instances. No details of the sizes of excision, or of the time taken to healing were given in this paper. However, closure of the defects by means of skin grafts appeared to be relatively successful, although it must be noted that grafts were only used where a superficial excision had been necessary.

Pollock, Virnelli and Ryan (1972) undermined the edges of their wounds following excision and then closed the wounds primarily. Of the 20 wounds, 12 healed primarily. Skin healing was delayed in 7 with areas of serous drainage; healing being completed by the 18th day. Significant central breakdown occurred in one wound. Full arm mobilisation (180° of abduction) was usually obtained by 6 weeks (range 4 - 9 weeks).

Tasche, Angelats and Jayaram (1975) started to use the Pollock procedure from 1972. Prior to this they had used Z-plasty, small excisions with primary closure, rotation flaps, primary and delayed split skin grafting. They found Z-plasty to be unsuccessful; rotation and transposition flaps generally worked well, but when they failed a long priod of time was required for secondary healing and grafting. Split skin grafting, both primary and secondary, was considered unsuccessful.

In view of our unit's previous successful experience with delayed split skin grafting in other situations (Rees and Hughes 1975) and the indifferent results obtained with rotation flaps/primary closure, we resolved to compare the use of delayed split skin grafting with healing by granulation utilising Silastic Foam dressing.

The median time to complete healing was 7 weeks for the grafted axillae and 12 weeks for the Silastic dressed axillae. At a median follow up period of 53.5 months, there has been no instance of wound contracture, limb swelling, or residual limitation of upper limb abduction.

Our incidence of skin graft loss was greater than that of Knaysi,

Cosman and Crikelair (1968) but they had only applied skin grafts to minor disease and the dimensions of their excisions were not given in the paper. Pollock, Virnelli and Ryan (1972) who performed excisions of the same order of magnititude as ours, implied that the longest time taken to full healing using their primary closure technique was the 18th post-operative day. This would clearly be a considerable improvement on our results, providing that the degree of severity of the disease that they were treating was as advanced as ours, and that when their follow up period was as long as ours, there was no limitation of arm movement or swelling.

In our experience, skin grafting had the following disadvantages:- it was necessary to immobilise the arm in an aeroplane splint until graft take was obtained; bilateral axillary excision necessitated bilateral arm immobilisation; a skin graft donor site which was initially painful and later left a cosmetic defect was unavoidable; there was an appreciable incidence of graft loss and finally the cosmetic appearance of the grafted axilla was inferior to that obtained with healing by granulation. The advantage of skin grafting was that where a successful take occurred, the healing time was shortened compared to healing by granulation; and this is reflected in the results obtained in the 10 patients acting as their own control. However, when graft failure occurs, then not only is this advantage lost, but subsequent healing by granulation is delayed. It may well be that the factors governing poor graft take and slow granulation are the same.

Pittam and Ellis (1984) have described a technique where following axillary excision, a split skin graft is immediately applied to the raw area and sutured to the margins, sides and floor of the defect with multiple interrupted 3/0 monofilament nylon sutures and tied firmly but not tightly. The graft is then fenestrated to allow sero-sanguineous collections to escape. The arm is supported in a sling for 24 hours and sutures are removed between 7 and 10 days later. Five patients had been treated in this manner at the time of their report, with at least 80% graft take. Antibiotic cover was used. This technique if largely successful in a greater number of patients would have the advantage of making

arm immobilisation unnecessary and hasten healing when compared to healing by granulation.

The solitary disadvantage of healing by granulation was the time taken to healing, which was slower than successful skin grafting. The advantages of healing by granulation included the certainty of healing, even though this was delayed in some cases; arm immobilisation was unnecessary; no skin graft donor site was inflicted upon the patient and the final cosmetic result was generally superior to that obtained by skin grafting.

Bilateral simultaneous axillary grafting is unacceptable to most patients because of the immobilisation involved. Healing by granulation, leaving the arms free, is, therefore, particularly applicable to bilateral axillary excisions.

It is clear that both healing by granulation and skin grafting were associated with advantages and disadvantages. Particular circumstances may indicate one or other technique especially in unilateral cases. The patients preferred healing by granulation, both on the grounds of relative comfort during healing and because of the ultimate appearance. As a result of patient preference, our standard approach now, is to allow the axillae to heal by granulation.

10.2 HEALING BY GRANULATION IN THE PUBO-INGUINO-PERINEAL REGION

Twenty-one patients underwent radical excision of the pubo-inguino-perineal region as previously defined. The wounds healed by granulation with a median healing time of 10 weeks. The cases treated by Barron (1970) with exteriorisation of the tracks, curettage and electrocoagulation took between 4 weeks and 2 months to heal completely, but areas of deeper excision could take longer. Thornton and Abcarian (1978) allowed their excisions to heal by granulation; the average time to full healing varying from 3 - 5 weeks for small wounds (2 x 2 cm.) to 7 weeks for large ones (more than 5 cm.). Ariyan and Krizek (1976) also allowed

the wounds to heal by granulation following wide excisions (no dimensions reported); complete epithelialisation taking place in 6 - 8 weeks. The latter authors made the point that the inguinal incisions healed with a linear scar and while wound contraction took place, wound contracture did not. While the above authors used healing by granulation in their series, none of them attempted complete excision of the apocrine glands in the region, and it is therefore likely that the dimensions of their excisions were much smaller than ours.

None of the patients in our series failed to heal by granulation, and supplementary skin grafts or flaps were unnecessary. The wounds healed with a linear scar in the lower abdomen, with a vertical extension on each side of the genitalia, much in the shape of the Greek figure π. The last areas to heal were the posterior perineal parts of the wound, and some tightness in this area was common immediately after healing but improved over the ensuing months until full hip abduction and external rotation at the hip were obtained.

The use of Silastic dressing obviated the need for gauze packing of the wounds. The major advantages of Silastic dressing over gauze packing were its non-adherent properties and its ease of patient self-management. Gauze however well soaked in Proflavine, Milton or half strength Eusol adheres to the underlying granulation tissue. Its removal, which is necessary on more than one occasion per day, causes pain and also causes the granulations to bleed. Silastic dressing can be lifted off easily causing minimal discomfort. It is not possible for a patient to effectively pack his own wound with gauze. This necessitates increased use of nursing services while in hospital and further demands upon the community nursing services after discharge. Within 4 - 5 days the patients learn to remove, clean and replace the Silastic dressing themselves and can continue to do this at home. All that is then necessary is a weekly visit to the Silastic dressing clinic to renew the dressing as the wound diminishes in size.

The use of Silastic dressing in the pubo-inguino-perineal region

resulted in effective healing with minimal patient discomfort and minimised the burden upon nursing services.

SECTION E

SUMMARY, CONCLUSIONS AND FINAL DISCUSSION

SUMMARY

SECTION B

CHAPTER III

3.1 AGE, SEX AND RACE.

Hidradenitis can arise at any time between the second and sixth decades of life. However, the second and third decades of life account for the majority of new cases in both males and females. There was a median interval of 6 years for the females and 8 years for the males between onset of the disease and the patients' presentation for its surgical excision.

A female predominance of 4:1 existed in this study, and the majority of the patients were of European origin.

3.2 SITE OF DISEASE.

The site most commonly involved by hidradenitis was the axilla in both sexes. The next most commonly involved site in both sexes was the pubo-inguino-perineal area, in particular, the groin. The involvement of other areas such as the inframammary folds, the skin over the sternum was seen in association with disease at the major sites, and only occurred in a small proportion of cases.

The male patients had a higher incidence of disease at multiple sites than the female patients. Hidradenitis could appear first in the axilla or the pubo-inguino-perineal region, and in the case of the axilla, its involvement could be bilateral (synchronous or metachronous) or unilateral.

3.3 TREATMENT RECEIVED PRIOR TO ENTRY INTO THE STUDY.

All the patients had received one or more courses of antibiotics prior to entering this study; 84% of these patients considered that antibiotics had not benefited them. The remainder had found that antibiotics limited the duration of acute exacerbations.

The bathing of involved sites with antiseptics had not been found to be useful.

Over half the patients had undergone multiple incision and drainage procedures, where pointing abscesses or inflammatory nodules existed. This had resulted in pain relief and abatement of that particular episode, but had failed to influence the recurrent nature of the disease.

These patients are not necessarily representative of hidradenitis patients as a whole, as the majority of these patients had active, chronic, progressive disease and were a selected population in which the previous management had failed.

CHAPTER IV

4.1 HIDRADENITIS AND IRON DEFICIENCY ANAEMIA.

There is no primary association between hidradenitis and iron deficiency anaemia. The anaemia reported by Tennant et al. (1968) is probably of the sort related to any case of long-term sepsis.

4.2 THE PREVALENCE OF DIABETES MELLITUS IN HIDRADENITIS PATIENTS AND THEIR FAMILIES.

Patients with hidradenitis do not exhibit an increased prevalence of diabetes mellitus nor is there an increased prevalence of diabetes mellitus in their family history.

4.3 A COMPARISON OF THE ABO AND RHESUS BLOOD GROUPS IN HIDRADENITIS PATIENTS, AS COMPARED TO THE PROPORTIONS OF THOSE GROUPS IN THE NORMAL POPULATION.

There was no significant difference in the distribution of ABO and Rhesus blood groups in hidradenitis patients as compared to normal controls.

4.4 FAMILY HISTORY OF HIDRADENITIS SUPPURATIVA IN HIDRADENITIS PATIENTS AS COMPARED TO NORMAL CONTROLS.

There was a significantly increased family history of hidradenitis suppurativa amongst hidradenitis patients as compared to a normal population. This could be explained by either common genetic or environmental factors.

4.5 THE PREVALENCE OF ACNE VULGARIS, SEBACEOUS (EPIDERMOID) CYSTS, IN HIDRADENITIS PATIENTS, AS COMPARED TO A CONTROL POPULATION.

There was a significantly increased prevalence of acne vulgaris and epidermoid cysts in hidradenitis patients as compared to a control population. This would support the concept that the basic lesion in hidradenitis is follicular occlusion probably caused by hyperkeratotic plugging.

4.6 THE PREVALENCE OF HYPERSENSITIVITY REACTIONS IN HIDRADENITIS PATIENTS, AS COMPARED TO NORMAL CONTROLS.

Hidradenitis patients do not show an increased prevalence of hypersensitivity reactions as compared to a control population. It is unlikely, therefore, that a hypersensitivity reaction is involved in the aetiology of hidradenitis.

4.7 THE USE OF DEPILATION, DEODORANTS AND TALCUM POWDER IN HIDRADENITIS PATIENTS PRIOR TO THE ONSET OF THE DISEASE, AS COMPARED TO NORMAL CONTROLS.

There were no significant differences in the use of mechanical shaving, chemical depilatory agents and deodorants, in hidradenitis patients prior to the onset of the disease, as compared to normal controls. While this does not exclude a role for these agents as triggering factors in susceptible subjects, it suggests that they are not primary factors causing follicular occlusion. There is probably some underlying abnormality in the anatomy or in the products of the pilo-sebaceous apparatus in hidradenitis subjects.

4.8 THE INFLUENCE OF MENSTRUAL PERIODS AND PREGNANCY UPON HIDRADENITIS.

The appearance of hidradenitis after puberty, its maximum incidence during the reproductive years and its decline during the climacteric, suggest an endocrine influence upon the activity of the disease. In this study, approximately one third of the women reported an exacerbation of their disease pre-menstrually, and approximately half of the women who had experienced a pregnancy during the course of the disease, reported disease remission during pregnancy. This indirect evidence of an endocrine influence is not conclusive, but does suggest that poorly understood endocrine influences exert an effect at the level of the pilo-sebaceous apparatus.

SECTION D

CHAPTER V

5.(1+2) SURFACE AREA, DIAMETER AND NUMBER OF APOCRINE GLANDS IN THE AXILLA AND PUBO-INGUINO-PERINEAL AREA.

There were no significant differences in the numbers, diameters or surface area of the apocrine glands in the axillary skin, when hidradenitis and control patients were compared. However, while there was no increase in the number of apocrine glands in the axillary skin of hyperhidrosis subjects as compared to controls and hidradenitis patients; the diameter and surface area of the apocrine glands in hyperhidrosis were significantly increased as compared to the other two groups. The increase in size of the apocrine glands in hyperhidrosis probably reflects an influence leading to their maximal growth potential.

Apocrine glands were few in number in the skin taken from over the pubic tubercle, in both hidradenitis patients and controls. However, there were no differences in the number, diameter or surface area of the glands in the skin taken from this area, when hidradenitis patients and controls were compared.

CHAPTER VI

6.1 A METHOD FOR THE PRE-OPERATIVE MAPPING OF THE APOCRINE GLANDS

The atropine/iodine/starch and oxytocin method demonstrated the distribution of the apocrine glands in the absence of eccrine sweating.

In the axilla, the sweating was most dense at the centre of the hair bearing area, with a declining density toward the periphery. Apocrine glands could be demonstrated to occur outside of the hair bearing area, in a scattered isolated fashion. The method did not materially influence the size of excision for axillary hidradenitis, which had been based upon excision of the hair bearing of the axilla, plus all visible disease, with a surrounding 2 cm. margin of normal skin.

In the pubo-inguino-perineal region, apocrine glands were demonstrated to be concentrated in the medial groins, extending into the perineum, pubic area, and the labium majus in the female and the scrotum in the male. Isolated scattered glands could be seen over the abdomen. The method led to a more standardised extent of excision in the pubo-inguino-perineal area, aimed at removing the major concentrations of apocrine glands.

The distribution of the apocrine glands as demonstrated by the atropine/iodine/starch and oxytocin method was confirmed by microscopic examination of the excised skin.

CHAPTER VII

7.1 MICROSCOPIC EXAMINATION OF RADICALLY EXCISED AXILLARY SPECIMENS.

Microscopic examination of axillary specimens excised from both hidradenitis patients and from cadavers who had not suffered from hidradenitis, demonstrated that the apocrine glands were most dense in the centre of the hair bearing area, with a progressively

declining gradient towards the periphery. Wide excisions of the hair bearing area of the axilla and surrounding skin are necessary to maximise the changes of completely ablating the axillary apocrine glands.

7.2 THE DISTRIBUTION OF THE APOCRINE GLANDS IN THE PUBO-INGUINO-PERINEAL REGION.

Microscopic examination of the excised pubo-inguino-perineal specimens showed that the apocrine glands were situated in the medial halves of the groins, adjacent thigh, pubis and perineum. In the female, apocrine glands were present in the labium majus, and in the male, they were present in the scrotal skin adjacent to the groin, and in the skin around the root of the penis.

CHAPTER VIII

8.1 THE MICROSCOPIC STUDY OF AREAS OF SKIN SHOWING THE MACROSCOPIC CHANGES OF HIDRADENITIS.

Apocrine glands were absent in the skin taken from the nape of the neck, the inframammary folds of the breasts and from over the sternum, which showed the macroscopic appearance of hidradenitis. Apocrine glands were sparse in number in the healthy and diseased area of the pubo-inguino-perineal region, the second most commonly involved site by hidradenitis. Whereas, hair follicles, eccrine and sebaceous glands were frequently seen, suggesting that the apocrine glands had not been destroyed by the disease process.

In no specimen could the inflammatory cells in the diseased area be seen to be confined to the apocrine glands, either in an intra-luminal position or in a periglandular position. The inflammatory cells were distributed throughout the subcutis, surrounding apocrine, eccrine, sebaceous glands and hair follicles equally.

Microscopic examination of the diseased skin was unable to confirm or refute the hypothesis that the apocrine glands are of primary importance in the pathogenesis of hidradenitis. Indeed, the

changes seen could possibly be explained by follicular occlusion secondary to hyperkeratotic plugging.

SECTION D

CHAPTER IX

9.1 RADICAL EXCISION OF THE AXILLARY SKIN.

Excision of the hair bearing area of the axilla with a 2 cm. margin of surrounding skin, or alternatively that area which has been demonstrated by the atropine/iodine/starch and oxytocin method to contain apocrine glands is an effective method of curing axillary hidradenitis.

9.2 RADICAL EXCISION OF THE PUBO-INGUINO-PERINEAL SKIN.

Excision of the main concentrations of apocrine glands in the pubo-inguino-perineal area, as previously described will control the majority of cases of hidradenitis in this region. However, a low rate of isolated recurrence at the margins of excision can be expected.

CHAPTER X

10.1 A COMPARISON OF SKIN GRAFTING VERSUS HEALING BY GRANULATION, FOLLOWING AXILLARY EXCISION FOR HIDRADENITIS.

Both healing by granulation with the use of Silastic Foam dressing or by split skin grafting following radical axillary excision are associated with advantages and disadvantages. Where a successful graft take is obtained, then grafting has the advantage that healing is relatively rapid. However, its disadvantages are that a painful donor site, which also leaves a cosmetic blemish is necessary; immobilisation of the ipsilateral arm is necessary while graft adherence occurs; and when graft failure occurs, healing is prolonged. The advantages of healing by granulation with the

use of Silastic Foam dressing are that a skin donor site is unnecessary; arm immobilisation is unnecessary; healing is certain and the patient can soon attend to their own management. Its disadvantage is that the time to heal is prolonged compared to a successful graft take. It is particularly suitable where bilateral axillary excision is to be performed synchronously.

Wound contracture and limb swelling did not occur in either group post-operatively.

10.2 HEALING BY GRANULATION IN THE PUBO-INGUINO-PERINEAL REGION.

None of the patients failed to heal by granulation, following radical excision of the pubo-inguino-perineal region, and supplementary skin grafts or flaps were unnecessary. The wounds healed with an acceptable cosmetic appearance; the median time to healing being 10 weeks. Some tightness in the post perineal part of the excision was common immediately following healing but this improved over the ensuing months and full hip abduction and external rotation was obtained in all cases. Patient discomfort was minimal and the use of Silastic Foam dressing minimised the demand upon nursing services.

CONCLUSIONS AND FINAL DISCUSSION

Hidradenitis suppurativa affects both males and females during the reproductive phase of life. It most commonly affects the axilla followed by the pubo-inguinal area. The evidence obtained from microscopy and the disease's association with acne vulgaris and epidermoid cysts points to it being a disease of the pilo-sebaceous apparatus.

Previous work by other authors suggests that the apocrine sweat glands are primarily involved by hidradenitis. This is supported by the presence of apocrine glands in the axilla and pubo-inguinal area, its association with Fox-Fordyce disease and Acanthosis Nigricans and by the experimental work of Shelley and Cahn (1955). However, microscopic examination of the diseased skin in this study was unable to clearly relate the inflammatory process to the apocrine glands alone. Furthermore, while apocrine glands are plentiful in the axilla, they are only sparsely distributed in the second most commonly involved site, the pubo-inguinal area. Hidradenitis or a variant of acne occurs in the inframammary and sternal areas where concentrations of apocrine glands were not found. The question as to whether the apocrine glands are primarily involved in hidradenitis remains unresolved.

The appearance of hidradenitis after the menarche and its tendency to disappear after the menopause, combined with exacerbations of the disease accompanying the menstrual periods and remissions during pregnancy suggests that endocrine factors are involved. This is supported by the fact that the incidence of hidradenitis decreases in later life, but the pilo-sebaceous units (including the apocrine glands) do not themselves disappear. Systemic studies have failed to reveal any consistent abnormality in hormone levels, but it is possible that abnormalities in hormone metabolism or transport at the level of the pilo-sebaceous unit are responsible for these observations. These changes would not be reflected by systemic studies. The level of systemic hormones, in particular, the sex hormones, in hidradenitis should themselves be re-investigated, with a view to determining the levels of the active moieties of the hormones, in addition to total levels. It is my opinion that this investigation should initially concentrate upon androgen

levels and metabolism.

This study has shown that the apocrine glands are normal in size and number in hidradenitis. Microscopy of the diseased skin revealed that hyperkeratosis was a marked feature and hyperkeratotic plugging of hair follicles was observed. Keratin formation is a complex process, still poorly understood, and studies of keratin formation in hidradenitis are indicated. The process of keratinisation may be influenced by the endocrine factors discussed above. The finding that an increased prevalence of a positive family history of hidradenitis exists in hidradenitis suggests that a genetically transmitted abnormality of the process of keratinisation, or of the anatomy of the apocrine duct or hair follicle may exist. Alternatively a common environmental agent could be involved.

Hidradenitis is not associated with diabetes mellitus, and the use of deodorants, depilatory agents and mechanical shaving are not primary aetiological factors.

The incidence of hidradenitis in the population remains unknown and further studies to determine its incidence are indicated. It has also been suggested that hidradenitis is associated with obesity. I have not studied this factor, but can state that this was not obvious in the patients in this study. The height and weight of hidradenitis patients should be compared with a control population.

This study shows that cure of chronic hidradenitis cannot be obtained by antibiotic therapy. Wide excision of the apocrine gland containing skin in the diseased area was effective in ablating hidradenitis in the axilla, but was less so in the pubo-inguino-perineal area. However, it is difficult to see that this method of treatment can be improved upon until there is a better understanding of the pathogenesis of hidradenitis, which may in turn lead to medical therapy effective in the early stages of the disease.

Healing of the axillary defects can be obtained by both skin grafting and healing by granulation. Grafting resulted in faster

healing, when successful, but better cosmesis was achieved by healing by granulation. Delayed skin grafting was used in this study, and a relatively high graft take failure rate was experienced. Use of primary grafting as recently described by Pittam and Ellis (1984) may produce more reliable results, without the need for arm immobilisation. However, this technique would still involve the cosmetic blemish of a skin graft donor site, which can be avoided by healing by granulation. In the pubo-inguino-perineal region healing by granulation gives certain healing and a good cosmetic result. I consider that the results obtained in this region make healing by granulation the best available technique.

The use of the atropine/iodine/starch and oxytocin method for demonstrating the distribution of the apocrine glands in the axilla, pre-operatively, did not assist excisional surgery in this area, as much as was hoped. This was largely because the distribution of the apocrine glands matched that of the hair growing skin, and complete excisions of this area had been performed prior to the use of the technique. However, it was successful in the pubo-inguino-perineal area in demonstrating the sites of major apocrine gland concentration, which led to a larger and modified extent of excision in this region, designed to secure their ablation in one procedure.

When recurrence of hidradenitis occurs following surgery, it is presumably due either to the presence of ectopic apocrine glands or diseased pilo-sebaceous units, outwith the margins of excision.

REFERENCES

AAVIK OR. CHOLINESTERASES IN HUMAN SKIN. JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1955; 24 :103 - 106.

ADAMS JD, HAISTEN AS. PERIANAL HIDRADENITIS SUPPURATIVA. SURGICAL CLINICS OF NORTH AMERICA. 1972; 52 (2) :467 - 472.

AJAYI OOA, OLURIN EO. HIDRADENITIS SUPPURATIVA. WEST AFRICAN MEDICAL JOURNAL. 1970; 19 :173 - 175.

ALEXANDER SJ. SQUAMOUS CELL CARCINOMA IN CHRONIC HIDRADENITIS SUPPURATIVA. CANCER. 1979; 43 :745 - 748.

ANDERSON DK, PERRY AW. AXILLARY HIDRADENITIS. ARCHIVES OF SURGERY. 1975; 110 (1) :69 - 72.

ANDERSON MJ, DOCKERTY MB. PERIANAL HIDRADENITIS SUPPURATIVA. A CLINICAL AND PATHOLOGIC STUDY. DISEASES OF COLON AND RECTUM. 1958; 1 :23 - 31.

AOKI T. STIMULATION OF HUMAN AXILLARY APOCRINE SWEAT GLANDS BY CHOLINERGIC AGENTS. 1962; 38 :41 - 44.

ARIYAN S, KRIZEK TJ. HIDRADENITIS SUPPURATIVA OF THE GROIN, TREATED BY EXCISION AND SPONTANEOUS HEALING. JOURNAL OF PLASTIC AND RECONSTRUCTIVE SURGERY. 1976; 58 (1) :44 - 48.

ARMSTRONG DP, ET AL. AXILLARY HIDRADENITIS SUPPURATIVA. JOURNAL OF PLASTIC AND RECONSTRUCTIVE SURGERY. 1965; 36 (2) :200 - 206.

ARNOLD H.L. STRESS THERAPY (PIROMEN) FOR EARLY AXILLARY HIDRADENITIS. POSTGRADUATE MEDICINE. 1955; 17 :366 - 368.

BARRON J. THE SURGICAL TREATMENT OF PERIANAL HIDRADENITIS SUPPURATIVA. DISEASES OF COLON AND RECTUM. 1970; 13 (6) :441 - 443.

BECKETT EB, BOURNE GH, MONTAGNA W. HISTOLOGY AND CYTOCHEMISTRY OF HUMAN SKIN. THE DISTRIBUTION OF CHOLINESTERASE IN THE FINGER OF THE EMBRYO AND THE ADULT. JOURNAL OF PHYSIOLOGY (LONDON). 1956; 134 :202 - 206.

BEIGELMAN PM, RANTZ LA. CLINICAL SIGNIFICANCE OF BACTEROIDES. ARCHIVES OF INTERNAL MEDICINE. 1949; 84 :605 - 631.

BELL BA, ELLIS H. HYDRADENITIS SUPPURATIVA. JOURNAL OF THE ROYAL SOCIETY OF MEDICINE. 1978; 71 :511 - 515.

BERGERON JR, STONE OJ. INTERSTITIAL KERATITIS ASSOCIATED WITH HIDRADENITIS SUPPURATIVA. ARCHIVES OF DERMATOLOGY. 1967; 95 :473 - 475.

BORSETTO PL. OSSERVAZIONI SULLO SVILUPPO DELLE GHIANDOLE SUDORIPARE NELLE DIVERSE REGIONI DELLA CUTE UMANA. ARCH. ITAL. ANAT. E EMBRIOL. 1951; 56 :332 - 348.

BRENNER DE, LOOKINGBILL DP. ANAEROBIC MICRO-ORGANISMS IN CHRONIC SUPPURATIVE HIDRADENITIS. LANCET. 1980; 25,2(8200) :921 - 992.

BRUNSTING HA. HIDRADENITIS SUPPURATIVA: ABSCESS OF THE APOCRINE SWEAT GLANDS. ARCH. DERM. SYPH. (NEW YORK). 1939; 39 :108 - 120.

BRUNSTING HA. HIDRADENITIS AND OTHER VARIANTS OF ACNE. ARCH. DERM. SYPH. 1952; 65 (3) :303 - 315.

BUNTING H. CYTOCHEMICAL PROPERTIES OF APOCRINE SWEAT GLANDS NORMALLY PRESENT IN THE HUMAN MAMMARY GLAND. ANAT. REC. 1948; 101 :5 - 12.

BUNTING H, WISLOCKI GB, DEMPSEY EW. THE CHEMICAL HISTOLOGY OF HUMAN ECCRINE AND APOCRINE SWEAT GLANDS. ANAT. REC.1948; 100 :61 - 77.

CAHN MM, SHELLEY WB. HYALURONIDASE-METHYLENE BLUE STAINING OF NERVE FIBRES ABOUT THE HUMAN AXILLARY APOCRINE SWEAT GLAND. JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1955; 25 :63 - 66.

CARTER AE. HIDRADENITIS SUPPURATIVA MASQUERADING AS PERINEAL URINARY FISTULAE. BRITISH JOURNAL OF SURGERY. 1962; 49 :686 - 687.

CAVAZZANA P. INDAGINI SUL COMPORTAMENTO MORFO-FUNZIONALE DELLE GHIANDOLE GLOMERULARI APOCRINE DELLA PELLE E DELL'ASCELLA DURANTE

LE FASI DEL CICLO MESTRUALE E NELLA GRAVIDANZA. RIV. ITAL. GINECOL. 1947; 30 :114 - 134.

CHALFANT WP, NANCE FC. HIDRADENITIS SUPPURATIVA OF THE PERINEUM: TREATMENT BY RADICAL EXCISION. THE AMERICAN SURGEON. 1970; 36 (6) :331 - 334.

CHAPMAN J. THE SURGICAL TREATMENT OF HIDRADENITIS SUPPURATIVA. JOURNAL OF THE NATIONAL MEDICAL ASSOCIATION. 1972; 64 :328 - 330.

CHARLES A. AN ELECTRON MICROSCOPIC STUDY OF THE HUMAN AXILLARY APOCRINE GLAND. JOURNAL OF ANATOMY. 1959; 93 :226 - 232.

CHEATLE GL, CUTLER M. TUMOURS OF THE BREAST, THEIR PATHOLOGY, SYMPTOMS, DIAGNOSIS AND TREATMENT. J.B. LIPPINCOTT, PHILADELPHIA. 1931.

CHING CC, STAHLGREN LH. A CLINICAL REVIEW OF HIDRADENITIS SUPPURATIVA: MANAGEMENT OF CASES WITH SEVERE PERIANAL INVOLVEMENT. DISEASES OF COLON AND RECTUM. 1965; 8 :349 - 352.

CHRISTENSEN JB. HIDRADENITIS SUPPURATIVA INVOLVING THE PARA-ANAL REGION. AMERICAN JOURNAL OF SURGERY. 1950; 79 :61 - 65.

CLEE W. THESIS ON THE APOCRINE SWEAT GLANDS. DEPT. OF ANATOMY, UNIVERSITY COLLEGE, CARDIFF. 1975.

CLEMMENSEN OJ. TOPICAL TREATMENT OF HIDRADENITIS SUPPURATIVA WITH CLINDAMYCIN. INTERNATIONAL JOURNAL OF DERMATOLOGY. 1983; 22 :325 - 328.

COCKE WM. SURGERY OF HIDRADENITIS SUPPURATIVA OF THE PERINEUM. PLASTIC AND RECONSTRUCTIVE SURGERY. 1967; 39 (2) :178 - 181.

CONWAY H, STARK RB, CLIMO S, WEETER JC, GARCIA FA. THE SURGICAL TREATMENT OF CHRONIC HIDRADENITIS SUPPURATIVA. SURGERY, GYNECOLOGY AND OBSTETRICS. 1952; 95 :455 - 464.

CORNBLEET T. TESTOSTERONE FOR APOCRINE DISEASES. HIDROSADENITIS, FOX-FORDYCE DISEASE. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY. 1952a; 65 (5) :549 - 552.

CORNBLEET T. PREGNANCY AND APOCRINE GLAND DISEASES. HIDRADENITIS, FOX-FORDYCE DISEASE. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY. 1952b; 65 (1) :12 - 19.

CULP CE. CHRONIC HIDRADENITIS SUPPURATIVA OF THE ANAL CANAL. DISEASE OF COLON AND RECTUM. 1983; 26 (10) :669 - 676.

CURTIS AC. IN DISCUSSION ON WILE UJ. AND CURTIS AC. CUSHING'S SYNDROME WITH HIDRADENITIS SUPPURATIVA. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY. 1948; 58 :746 - 747.

DACIE JV, LEWIS SM. PRACTICAL HAEMATOLOGY. 6TH EDITION CHURCHILL/ LIVINGSTONE. EDINBURGH/LONDON. 1984.

DANTO JL. PRELIMINARY STUDIES OF THE EFFECT OF HYDROCORTISONE ON HIDRADENITIS SUPPURATIVA. JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1958; 31 :299 - 300.

DARLEY CR. RECENT ADVANCES IN HORMONAL ASPECTS OF ACNE VULGARIS. INTERNATIONAL JOURNAL OF DERMATOLOGY. 1984; 23 (8) :539 - 541.

DARROW CW. THE RELATION OF THE GALVANIC SKIN REFLEX RECOVERY CURVE TO REACTIVITY, RESISTANCE LEVEL AND PERSPIRATION. J. GEN. PSYCHOL. 1932; 7 :261 - 273.

DAWSON EK. SWEAT GLAND CARCINOMA OF BREAST: MORPHO-HISTOLOGICAL STUDY. EDINBURGH MEDICAL JOURNAL. 1932; 39 :409 - 438.

DONSKY HJ, MENDELSON CG. SQUAMOUS CELL CARCINOMA AS A COMPLICATION OF HIDRADENITIS SUPPURATIVA. ARCHIVES OF DERMATOLOGY. 1964; 90 :488 - 491.

DOTY RL, ORNDORFF MM, LEYDEN J, KLIGMAN A. COMMUNICATION OF GENDER FROM HUMAN AXILLARY ODORS: RELATIONSHIP TO PERCEIVED INTENSITY

AND HEDONICITY. BEHAVIORAL BIOLOGY. 1978; 23 :373 - 380.

DUNCAN WC. SURGICAL TREATMENT OF HIDRADENITIS SUPPURATIVA. JOURNAL OF DERMATOLOGICAL SURGERY. 1976; 2 (2) :153 - 157.

DVORAK VC, ROOT RK, MACGREGOR RR. HOST-DEFENSE MECHANISMS IN HIDRADENITIS SUPPURATIVA. ARCHIVES OF DERMATOLOGY. 1977; 113 :450 - 453.

ELLIS RA, MONTAGNA W, FANGER H. HISTOLOGY AND CYTOCHEMISTRY OF HUMAN SKIN, XIV. THE BLOOD SUPPLY OF THE CUTANEOUS GLANDS. JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1958; 30 :137 - 140.

ELLIS RA. ECCRINE, SEBACEOUS AND APOCRINE GLANDS. IN ZELICKSON AS, ed. ULTRASTRUCTURE OF NORMAL AND ABNORMAL SKIN. PHILADELPHIA, LEA AND FEBIGER, 1967 :132 - 162.

ESTERLY NB, OPPENHEIMER EH, ESTERLY JR. OBSERVATIONS ON CYSTIC FIBROSIS OF THE PANCREAS. AMERICAN JOURNAL OF DISEASES OF CHILDREN. 1972; 123 :200 - 203.

FANGER H, BARKER BE. PHOSPHORYLASE AND AMYLO-1, 6-GLUCOSIDASE IN BREAST TISSUE. JOURNAL OF THE NATIONAL CANCER INSTITUTE. 1960; 24 :691 - 697.

FISCHER E. CHANGES IN BIFRINGENCE DURING CONTRACTION AND STRETCH OF SMOOTH MUSCLE. JOURNAL OF CELLULAR AND COMPARITIVE PHYSIOLOGY. 1936; 8 :503 - 514.

FOOTE FW, STEWART FW. COMPARATIVE STUDIES OF CANCEROUS VERSUS NONCANCEROUS BREASTS. ANNALS OF SURGERY. 1945; 121 :6 - 53, 197 - 222.

FOX RH, MULLAN BJ, THORNTON C. A TECHNIQUE FOR STUDYING APOCRINE GLAND FUNCTION IN MAN. PROCEEDINGS OF THE PHYSIOLOGICAL SOCIETY. 1974; Feb:75P - 76P.

GESCHICKTER CF. DISEASES OF THE BREAST: DIAGNOSIS, PATHOLOGY, TREATMENT. 2ND EDITION. PHILADELPHIA, JB. LIPPINCOTT: 1945.

GIACOMETTI L, MONTAGNA W. THE NIPPLE AND AREOLA OF THE HUMAN FEMALE BREAST. ANAT. REC. 1962; 144 :191 - 197.

GINDER PA, OUSLEY M, HINTHORN D, LIU C, ABDOU NI. HIDRADENITIS SUPPURATIVA: EVIDENCE FOR A BACTERICIDAL DEFECT CORRECTABLE BY CHOLINERGIC AGONIST IN VITRO AND IN VIVO. JOURNAL OF CLINICAL IMMUNOLOGY. 1982; 2 (3) :237 - 241.

GOLDSMITH WN. HIDRADENITIS SUPPURATIVA (APOCRINE ACNE). BRITISH JOURNAL OF DERMATOLOGY AND SYPHILOLOGY. 1950; 62 (7 - 8) :327 - 329.

GOLDZEIHER MA, KALDOR J. CYSTIC CIRRHOSIS OF BREAST. ARCHIVES OF SURGERY. 1930; 20 :473 - 490.

GORDON SW. HIDRADENITIS SUPPURATIVA: A CLOSER LOOK. J. NATL. MED. ASSOC. 1978; 70 (5) :339 - 343.

GREELY PW. SURGICAL TREATMENT OF CHRONIC SUPPURATIVE HIDRADENITIS. ARCHIVES OF SURGERY. 1950; 61 (2) :193 - 198.

GREELY PW. PLASTIC SURGICAL TREATMENT OF CHRONIC SUPPURATIVE HIDRADENITIS. PLASTIC AND RECONSTRUCTIVE SURGERY. 1951; 7 :143 - 146.

GREER KE. FACIAL INVOLVEMENT WITH HIDRADENITIS SUPPURATIVA. ARCHIVES OF DERMATOLOGY. 1974; 109: 408 - 410.

HARRISON SH. AXILLARY HIDRADENITIS. BRITISH JOURNAL OF PLASTIC SURGERY. 1964; 17 :95 - 98.

HARWELL SW. SURGICAL TREATMENT OF HIDRADENITIS SUPPURATIVA. SURGICAL CLINICS OF NORTH AMERICA. 1975; 55 (5) :1107 - 1108.

HASHIMOTO K, GROSS BG, LEVER WF. AN ELECTRON MICROSCOPIC STUDY OF THE ADULT HUMAN DUCT. JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1966; 46 (1) :6 - 11.

HERZENBURG H. NEUE BEITRAGE ZUE LEHRE VON DEN APOKRINEN SCHWEISSDRUSEN. VIRCH. ARCH. f.PATH.ANAT.u.PHYSIOL. 1927; 266 :422 - 425.

HEWER EE. TEXTBOOK OF HISTOLOGY FOR MEDICAL STUDENTS. 9TH EDITION. 1969. LONDON. HEINEMANN.

HIGHET AS, ROBERTS SOB, WARREN RE, STAUGHTON RCD. PERINEAL SUPPURATIVE HIDRADENITIS. LANCET. 1980; 2 (8205) :1203.

HOMMA H. ON APOCRINE SWEAT GLANDS IN WHITE AND NEGRO MEN AND WOMEN. BULLETIN JOHN HOPKINS HOSPITAL. 1926; 38 :385 - 371.

HORNER WE. ON THE ODORIFEROUS GLANDS OF THE NEGRO. AMERICAN JOURNAL OF MEDICAL SCIENCE. 1846; 21 :13 -16.

HURLEY HJ, SHELLEY WB, KOELLE GB. THE DISTRIBUTION OF CHOLINESTERASES IN HUMAN SKIN, WITH SPECIAL REFERENCE TO ECCRINE AND APOCRINE SWEAT GLANDS. JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1953; 21 :139 - 142.

HURLEY HJ, SHELLEY WB. APOCRINE SWEAT RETENTION IN MAN. I. EXPERIMENTAL PRODUCTION OF ASYMPTOMATIC FORM. JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1954; 22 :397 - 404.

HURLEY HJ, SHELLEY WB. THE HUMAN APOCRINE SWEAT GLAND IN HEALTH AND DISEASE. 1960. SPRINGFIELD, ILLINOIS. THOMAS.

HYLAND WT, NEALE HW. SURGICAL MANAGEMENT OF CHRONIC HIDRADENITIS SUPPURATIVA OF THE PERINEUM. SOUTHERN MEDICAL JOURNAL. 1976; 69 (8) :1002 - 1004.

INQUE T. SCANNING ELECTRON MICROSCOPIC STUDY OF THE HUMAN AXILLARY APOCRINE GLANDS. JOURNAL OF DERMATOLOGY (TOKYO). 1979; 6 (5) :299 - 308.

ITO T, TSUCHIYA K, IWASHIGE K. STUDIEN UBER DIE BASOPHILE SUBSTANZ (RIBONUKLEINSAURE) IN DEN ZELLEN DER MENSCHLICHEN SCHWEISSDRUSEN. ARCH. ANAT. JAP. 1951; 2 :279 - 287.

JACKMAN RJ. HIDRADENITIS SUPPURATIVA: DIAGNOSIS AND TREATMENT OF ITS PERIANAL MANIFESTATIONS. AMERICAN JOURNAL OF DIGESTIVE DISEASES. 1942; 9 (7) :220 - 222.

JACKMAN RJ, MCQUARRIE HB. HIDRADENITIS SUPPURATIVA: ITS CONFUSION WITH PILONIDAL DISEASE AND ANAL FISTULA. AMERICAN JOURNAL OF SURGERY. 1949; 77 :349 - 351.

JONES DH, CUNLIFFE WJ, KING K. HIDRADENITIS SUPPURATIVA - LACK OF SUCCESS WITH 13 CIS-RETINOIC ACID. BRITISH JOURNAL OF DERMATOLOGY. 1982; 107 (2) :252 (letter).

KLIGMAN AM, SHEHADEH N. PUBIC APOCRINE GLANDS AND ODOR. ARCHIVES OF DERMATOLOGY. 1964; 89 (3) :461 - 463.

KNAYSI GA, COSMAN B, CRIKELAIR GF. HIDRADENITIS SUPPURATIVA. JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. 1968; 203(1) :73 - 76.

KOELLE GB. THE ELIMINATION OF ENZYMATIC DIFFUSION ARTEFACTS IN THE HISTOCHEMICAL LOCALISATION OF CHOLINESTERASES AND A SURVEY OF THEIR CELLULAR DISTRIBUTIONS. J. PHARM. EXP. THER. 1951; 103 :153 - 171.

KOLLIKER A. IN MANUAL OF HUMAN HISTOLOGY. BUSK G, HUXLEY T. EDS. 1853; VOL. 1: LONDON, SYDENHAM SOCIETY.

KRAUSE C. HAUT. WAGNER'S HANDBOOK OF PHYSIOLOGY. 1844; 2 : 108. QUOTED BY MONTAGNA W. THE STRUCTURE AND FUNCTION OF SKIN. CHAPTER 7. THE APOCRINE SWEAT GLANDS. 1962; 2ND EDITION: 374 - 421. NEW YORK, ACADEMIC PRESS.

KRESS DW, GRAHAM WP, DAVIS TS, MILLER SH. A PRELIMINARY REPORT ON THE USE OF STAPHAGE LYSATE FOR THE TREATMENT OF HIDRADENITIS SUPPURATIVA. ANNALS OF PLASTIC SURGERY. 1981; 6(5) :393 - 395.

KROMPECHER E. ZUR KENNTNIS DER GESCHWULSTE UND HYPERTROPHEN DER SCHWEISZDRUSEN. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY. 1919; 126 : 765.

KUNO Y. HUMAN PERSPIRATION. 1956; SPRINGFIELD, THOMAS.

LABOWS JN, PRETI G, HOELZLE E, LEYDEN J, KLIGMAN A. STEROID ANALYSIS OF HUMAN APOCRINE SECRETION. STEROIDS. 1979; 34(3) :249 - 257.

LEACH RD, EYKYN SJ, PHILLIPS I, CORRIN B. ANAEROBIC SUBAREOLAR BREAST ABSCESS. LANCET. 1979; 1(8106) :35 - 37.

LEE BJ, PACK GT, SCHARNAGEL I. SWEAT GLAND CANCER OF THE BREAST. SURGERY, GYNECOLOGY AND OBSTETRICS. 1933; 56 :975 - 996.

LETTERMAN G, SCHURTER M. SURGICAL TREATMENT OF HYPERHIDROSIS AND CHRONIC HIDRADENITIS SUPPURATIVA. JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1974; 63 (1) :174 - 182.

LIPSHUTZ H. CLOSURE OF AXILLARY HIDRADENITIS DEFECTS WITH LOCAL TRIANGULAR FLAPS. 1974; 53 (6) :677 - 679.

LOBITZ WC, CAMPBELL CJ. PHYSIOLOGY OF THE GLANDS OF THE HUMAN EAR CANAL: A PRELIMINARY REPORT. JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1952; 19 :125 - 135.

LOESCHCKE H. UBER ZYKLISCHE VORGANGE IN DEN DRUSEN DES ACHSELHOHLENORGANS UND IHRE ABHANGIGKEIT VOM SEXUALZYKLUA DES WEIBES. VIRCHOWS ARCHIVES OF ANATOMY. 1925; 255 :283 - 294.

LORINCZ AL, LANCASTER GL. ANTERIOR PITUITARY PREPARATION WITH TROPIC ACTIVITY FOR SEBACEOUS, PREPUTIAL AND HARDERIAN GLANDS. SCIENCE. 1957; 126 (3264) :124 - 125.

MACKENNA RMB, LEHMANN H. THE GLUCOSE TOLERANCE CURVE IN HIDRADENITIS SUPPURATIVA. BRITISH JOURNAL OF DERMATOLOGY. 1960; 72 :142 - 144.

MARKS MM. FAILURE OF LIPID METABOLISM: PROCTOLOGIC SIGNIFICANCE. SOUTHERN MEDICAL JOURNAL. 1945; 39 (6) :477 - 480.

MASSON JK. SURGICAL TREATMENT FOR HIDRADENITIS SUPPURATIVA. SURGICAL CLINICS OF NORTH AMERICA. 1969; 49 (5) :1043 - 1052.

McDANIEL DH, WELTON WA. FURUNCULOSIS AND HIDRADENITIS SUPPURATIVA RESPONSE. ARCHIVES OF DERMATOLOGY. 1984; 120 :437 (Letter).

MINAMITANI K. ZYTOLOGISCHE UND HISTOLOGISCHE UNTERSUCHUNGEN DER

SCHWEISS DRUSEN IN MENSCHLICHER ACHSELHAUT UBER DAS VORKOMMEN DER BESONDEREN FORMEN DER APOKRINEN UND EKKRINEN SCHWEISSDRUSEN IN ACHSELHAUT VON JAPANERN. OKAJIMA'S FOLIA ANAT. JAPON. 1941; 20 :563 - 590.

MONTAGNA W, CHASE HB, LOBITZ WC. HISTOLOGY AND CYTOCHEMISTRY OF HUMAN SKIN. V. AXILLARY APOCRINE SWEAT GLANDS. AMERICAN JOURNAL OF ANATOMY. 1953; 92 (3) :451 - 470.

MONTAGNA W. AGEING OF THE AXILLARY APOCRINE SWEAT GLANDS IN THE HUMAN FEMALE. IN CIBA FOUNDATION COLLOQUIN ON AGEING. VOL. 2. AGEING IN TRANSIENT TISSUES. EDS. WOLSTENHOLME GEW, MILLER ECP. 1956. LONDON. CHURCHILL. 188 - 201.

MONTAGNA W, ELLIS RA. L'HISTOLOGIE ET LA CYTOLOGIE DE LA PEAU HUMAINE. XVI. REPARTITION ET CONCENTRATION DES ESTERASES CARBOXYLIQUES. ANN. HISTOCHIM. 1958; 3 :1 - 17.

MONTAGNA W. HISTOLOGY AND CYTOCHEMISTRY OF HUMAN SKIN. XIX. THE DEVELOPMENT AND FATE OF THE AXILLARY ORGAN. JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1959; 33 :151 - 161.

MONTAGNA W, ELLIS RA. THE SKIN OF PRIMATES. I. THE SKIN OF THE POTTO (PERODICTICUS POTTO). AMERICAN JOURNAL OF PHYSICAL ANTHROPOLOGY. 1959; 17 :137 - 162.

MONTAGNA W, ELLIS RA. HISTOLOGY AND CYTOCHEMISTRY OF HUMAN SKIN. XXI. THE NERVES AROUND THE AXILLARY APOCRINE GLANDS. AMERICAN JOURNAL OF PHYSICAL ANTHROPOLOGY. 1960 a; 18 :69 - 70.

MONTAGNA W, ELLIS RA. THE SKIN OF PRIMATES. II. THE SKIN OF THE SLENDER LORIS (LORIS TARDIGRADUS). AMERICAN JOURNAL OF PHYSICAL ANTHROPOLOGY. 1960 b; 18 :19 - 44.

MONTAGNA W. THE STRUCTURE AND FUNCTION OF SKIN. 2ND EDITION. CHAPTER 7. THE APOCRINE SWEAT GLANDS. 1962. NEW YORK, ACADEMIC PRESS :374 - 421.

MONTAGNA W. HISTOLOGY AND CYTOCHEMISTRY OF HUMAN SKIN. XXIV. FURTHER OBSERVATIONS ON THE AXILLARY ORGAN. JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1964; 42 :119 - 129.

MONTAGNA W, FORD DM. HISTOLOGY AND CYTOCHEMISTRY OF HUMAN SKIN. XXXIII. THE EYELID. ARCHIVES OF DERMATOLOGY. 1969; 100 :328 - 335.

MONTAGNA W, YUN JS. THE GLANDS OF MONTGOMERY. BRITISH JOURNAL OF DERMATOLOGY. 1972; 86 (2) :126 - 133.

MONTAGNA W, PARAKKAL PF. THE STRUCTURE AND FUNCTION OF SKIN. 3RD EDITION. CHAPTER 11. APOCRINE GLANDS. 1974. NEW YORK AND LONDON, ACADEMIC PRESS :332 - 363.

MONTES LF, BAKER BL, CURTIS AC. THE CYTOLOGY OF THE LARGE AXILLARY SWEAT GLANDS IN MAN. THE JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1960; 35 :273 - 283.

MOSCHELLA SL. HIDRADENITIS SUPPURATIVA. COMPLICATIONS RESULTING IN DEATH. JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. 1966; 198 (1) :201 - 203.

MULLINS JF, McCASH WB, BOUDREAU RF. TREATMENT OF CHRONIC HIDRADENITIS SUPPURATIVA: SURGICAL MODIFICATION. POSTGRADUATE MEDICINE. 1959; 26 :805 - 808.

MUSTAFA EB, ALI SD, KURTZ LH. HIDRADENITIS SUPPURATIVA: REVIEW OF THE LITERATURE AND MANAGEMENT OF THE AXILLARY LESION. J. NAT. MED. ASSOC. 1980; 72 (3) :237 - 243.

NANCE FC. HIDRADENITIS SUPPURATIVA OF THE PERINEUM, TREATED BY RADICAL EXCISION. AM. SURG. 1970; 36 :331 - 334.

NEWELL GB, VOELTER WW, MULLINS JF. TREATMENT OF HIDRADENITIS SUPPURATIVA. JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. 1973; 223 (5) :556.

NISHIO T. GENETIC STUDY ON THE APOCRINE GLAND IN THE JAPANESE. J. YONAGO MED. ASSOC. 1964; 15 :185 -208.

O'BRIEN J, WYSOCKI J, ANASTASI G. LIMBERG FLAP COVERAGE FOR AXILLARY DEFECTS RESULTING FROM EXCISION OF HIDRADENITIS SUPPURATIVA. PLASTIC AND RECONSTRUCTIVE SURGERY. 1976; 58(3) :354 - 358.

OGAWA H, YOSHIIKE T. KERATIN, KERATINIZATION AND BIOCHEMICAL ASPECTS OF DYSKERATOSIS. INTERNATIONAL JOURNAL OF DERMATOLOGY. 1984; 23 (8) :507 - 513.

PALETTA FX. HIDRADENITIS SUPPURATIVA. PATHOLOGIC STUDY AND USE OF SKIN FLAPS. PLASTIC AND RECONSTRUCTIVE SURGERY. 1963; 31 :307 - 315.

PERRY ET, HURLEY HJ, GRAY MB, SHELLEY WB. THE ADRENERGIC INNERVATION OF THE APOCRINE (CERUMINOUS) GLAND OF THE HUMAN EAR CANAL. JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1955; 25 :219 - 221.

PIGGOTT H, ELLIS H. CHRONIC HYDRADENITIS SUPPURATIVA: A REPORT OF 9 CASES. BRITISH JOURNAL OF SURGERY. 1975; 62 :394 - 396.

PINKUS H. EMBRYOLOGY OF HAIR, IN THE BIOLOGY OF HAIR GROWTH. EDS. MONTAGNA W, ELLIS RA. 1958. NEW YORK, ACADEMIC PRESS :1 - 32.

PITTAM MR, ELLIS H. A COMPARISON OF SKIN GRAFTING AND HEALING BY GRANULATION FOLLOWING AXILLARY EXCISION FOR HIDRADENITIS SUPPURATIVA. ANNALS OF THE ROYAL COLLEGE OF SURGEONS OF ENGLAND. 1984; 66 (1) :73 (Letter).

POLLOCK WJ, VIRNELLI FR, RYAN RF. AXILLARY HIDRADENITIS SUPPURATIVA. A SIMPLE AND EFFECTIVE SURGICAL TECHNIQUE. PLASTIC AND RECONSTRUCTIVE SURGERY. 1972; 49 :22 - 27.

PURKINJE - QUOTED BY KUNO Y. HUMAN PERSPIRATION. 1956. SPRINGFIELD, ILLINOIS. THOMAS.

RANVIER 1887 - QUOTED BY KUNO Y. HUMAN PERSPIRATION. 1956. SPRINGFIELD, ILLINOIS. THOMAS.

REBAUDI S. DER SCHWEISSDRUSEN - APPARAT WAHREND DER NORMALEN UND DER PATHOLOGISCHEN SCHWANGERSCHAFT. BEITR. ZUR GEBURTS. U. GYNAEK. 1921; 17 :11.

RECHARDT L, WARIS T, RINTALA A. INNERVATION OF HUMAN AXILLARY SWEAT GLANDS. SCANDINAVIAN JOURNAL OF PLASTIC AND RECONSTRUCTIVE SURGERY. 1976; 10 :107 - 112.

RICHTER W. BEITRAGE ZUR NORMALEN UND PATHOLOGISCHEN ANATOMIE DER APOKRINEN HAUTDRUSEN DES MENSCHEN MIT BESONDERER BERUCKSICHTIGUNG DES ACHSEL HOHLENORGANS. VIRCHOWS ARCHIVES. 1932; 287 :277 - 296.

ROBERTSHAW D. NEURAL AND HUMORAL CONTROL OF APOCRINE GLANDS. THE JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1974; 63 :160 - 167.

ROBIN C. NOTE SUR UNE ESPECE PARTICULIERE DE GLANDES DE LA PEAU DE L'HOMME. TROISIEME SERIE ZOOLOGIE. ANN. SC. NAT. PARIS. 1845; 4 :380.

ROLIN MC. SUDORIPAROUS GLANDS OF THE AXILLA. AMERICAN JOURNAL OF MEDICAL SCIENCE. 1846; 11 :439.

ROTHMAN S. PHYSIOLOGY AND BIOCHEMISTRY OF THE SKIN. 1954. CHICAGO, UNIVERSITY OF CHICAGO PRESS :180 - 188.

SACHS DD, GORDON AT. HIDRADENITIS SUPPURATIVA OF THE GLANDS OF MOLL. ARCHIVES OF OPHTHAMOLOGY. 1967; 77 :635 - 636.

SCHAUMBURG-LEVER G, LEVER WF. SECRETION FROM HUMAN APOCRINE GLANDS: AN ELECTRON MICROSCOPIC STUDY. JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1975; 64 :38 - 41.

SCHENCK SG. HIDRADENITIS SUPPURATIVA AXILLARIS. RADIOLOGY. 1950; 54 :74 - 77.

SCHIEFFERDECKER P. DIE HAUTDRUSEN DES MENSCHEN UND DER SAUGETIERE, IHRE BIOLOGISCHE UND RASSENANATOMISCHE BEDEUTUNG, SOWIE DIE MUSCULARIS SEXUALIS. BIOL. ZENTR. 1917; 37 :534 - 562.

SCHIEFFERDECKER P. DIE HAUTDRUSEN DES MENSCHEN UND DES SAUGETIERES, IHRE BEDEUTUNG, SOWIE DIE MUSCULARIS SEXUALIS. ZOOLOGICA. 1922; 72 :1 - 154.

SCHMITT FO. TISSUE ULTRASTRUCTURE ANALYSIS: POLARIZED LIGHT METHOD. MEDICAL PHYSICS YEAR BOOK. 1944. CHICAGO :1586 - 1591.

SHAUGHNESSY DM, GREMINGER RR, MARGOLIS IB, DAVIS C. HIDRADENITIS SUPPURATIVA: A PLEA FOR EARLY OPERATIVE TREATMENT. JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. 1972; 222 :320 - 321.

SHEHADEH NH, KLIGMAN AM. THE EFFECT OF TOPICAL ANTIBACTERIAL AGENTS ON THE BACTERIAL FLORA OF THE AXILLA. JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1963; 40 :61 - 71.

SHELLEY WB, HURLEY HJ. THE PHYSIOLOGY OF THE HUMAN AXILLARY APOCRINE SWEAT GLAND. JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1953; 20 :285 - 297.

SHELLEY WB, HURLEY HJ, NICHOLS AC. AXILLARY ODOR. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY. 1953; 68 :430 - 446.

SHELLEY WB, HURLEY HJ. LOCALIZED CHROMIDROSIS. A SURVEY. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY. 1954; 69 :449 - 468.

SHELLEY WB, CAHN MM. THE PATHOGENESIS OF HIDRADENITIS SUPPURATIVA IN MAN. ARCHIVES OF DERMATOLOGY. 1955; 72 :562 - 565.

SHELLEY WB, CAHN MM. EXPERIMENTAL STUDIES ON THE EFFECT OF HORMONES ON THE HUMAN SKIN WITH REFERENCE TO THE AXILLARY APOCRINE SWEAT GLAND. JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1955b; 25 :127 - 131.

SHELLEY WB, COHEN SB, KOELLE GB. HISTOCHEMICAL DEMONSTRATION OF MONOAMINE OXIDASE IN HUMAN SKIN. JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1955; 24 :561 - 565.

SHELLEY WB, BUTTERWORTH T. THE ABSENCE OF THE APOCRINE GLANDS AND HAIR IN THE AXILLA IN MONGOLISM AND IDIOCY. JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1955; 25 :165 - 167.

SMITH WE, ROPES MW. BACTEROIDES INFECTIONS. NEW ENGLAND JOURNAL OF MEDICINE. 1945; 232 :31 - 37.

SPILLER RF, KNOX JM. FOX-FORDYCE DISEASE WITH HIDRADENITIS SUPPURATIVA. JOURNAL OF INVESTIGATIVE DERMATOLOGY. 1958; 31 :127 - 135.

STEINER K, GRAYSON LD. HIDRADENITIS SUPPURATIVA OF THE ADULT AND ITS MANAGEMENT. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY. 1955; 71 :205 - 211.

STONE OJ. HIDRADENITIS SUPPURATIVA FOLLOWING ACANTHOSIS NIGRICANS. ARCHIVES OF DERMATOLOGY. 1976; 112 :1142.

SULZBERGER MB. IN DISCUSSION ON LUDY JB, DRANT P. HIDRADENITIS SUPPURATIVA, PAPULONECROTIC TUBERCULID AND BROMODERMIA. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY. 1941; 44 :494.

TACHAU P. ABSCESSES OF THE SWEAT GLANDS IN ADULTS. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY. 1939; 40 :595 - 600.

TAKAYASU S. METABOLISM AND ACTION OF ANDROGEN IN THE SKIN. INTERNATIONAL JOURNAL OF DERMATOLOGY. 1979; 18 :681.

TALKE L. UBER DIE GROSSEN DRUSEN DER ACHSELHOHLENHAUT DES MENSCHEN. ARCH. MIKROSK. ANAT. ENTWICKLUNGSMECH. 1903; 61 :537 - 555.

TASCHE C, ANGELATS J, JAYARAM B. SURGICAL TREATMENT OF HIDRADENITIS SUPPURATIVA OF THE AXILLA. PLASTIC AND RECONSTRUCTIVE SURGERY. 1975; 55 (5) :559 - 562.

TENNANT F, BERGERON JR, STONE OJ, MULLINS JF. ANAEMIA ASSOCIATED WITH HIDRADENITIS SUPPURATIVA. ARCHIVES OF DERMATOLOGY. 1968; 98 :138 - 140.

THIES W, GALENTE F. ZUR HISTOCHEMISCHEN DARSTELLUNG DER CHOLINESTERASEN IM VEGETATIVEN NERVENSYSTEM DER HAUT. HAUTARZT. 1957; 8 :69 - 75.

THIES W. DIE INNERVATION DER APOKRINEN DRUSEN. ACTA NEUROVEGETATIVA (WIEN). 1958; 18 (1-4) :191 - 202.

THORNTON JP, ABCARIAN H. SURGICAL TREATMENT OF PERIANAL AND PERINEAL HIDRADENITIS SUPPURATIVA. DISEASES OF THE COLON AND RECTUM. 1978; 21 (8) :573 - 577.

VELPEAU A. (1839 - 45) IN: DICTIONNAIRE DE MEDECINE, UN REPERTOIRE GENERAL DES SCIENCES MEDICALES SOUS LA RAPPORT THEORIQUE ET PRACTIQUE. 2ND EDITION. BECHET JEUNE: AISELLE 2; 91. ANUS 3; 304. MAMELLES 19; 1.

VERNEUIL A. ETUDES SUR LES TUMEURS DE LA PEAU ET QUELQUES MALADIES DES GLANDES SUDORIPARES. ARCH. GEN. MED. 1854; 4 :447 - 468, 693 - 705. DE L'HIDROSADENITE PHLEGMONEUSE ET DES ABCES SUDORIPARES. ARCH. GEN. MED. 1864; 114 :537. 1865; 115 :327, 437.

VICKERS MA. OPERATIVE MANAGEMENT OF CHRONIC HIDRADENITIS SUPPURATIVA OF THE SCROTUM AND PERINEUM. JOURNAL OF UROLOGY. 1975; 114 :414 - 416.

VOHWINKEL KH. UBER DAS VORKOMMEN VON APOKRINEN DRUSEN. DERMAT. ZTSCHR. 1931; 60 :314 - 321.

WADA M. SUDORIFIC ACTION OF ADRENALIN ON THE HUMAN SWEAT GLANDS AND DETERMINATION OF THEIR EXCITABILITY. SCIENCE. 1950; 111 :376 - 377.

WAELSCH L. UBER VERANDERUNGEN DER ACHSELSCHWEISSDRUSEN WAHREND DER GRAVIDITAT. ARCH. DERMATOL. SYPH. 1912; 114 :139 - 160.

WARD JN, WASHIO H, DAVID HS. HIDRADENITIS SUPPURATIVA OF THE SCROTUM AND PERINEUM. UROLOGY. 1974; IV (4) :463 - 466.

WAY SC, MEMMESHEIMER A. THE SUDORIPAROUS GLANDS. II. THE APOCRINE GLANDS. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY. 1938; 38 :373.

WEINER J, LEWIS JE, SAMITZ MH. HIDRADENITIS SUPPURATIVA OCCURRING ON THE LEG. CUTIS. 1976; 17 (5) :888 - 891.

WENDT, CITED BY KUNO Y. IN HUMAN PERSPIRATION. 1956. SPRINGFIELD, ILLINOIS. THOMAS.

WORLD HEALTH ORGANISATION EXPERT COMMITTEE ON DIABETES MELLITUS. (2ND REPORT).

WINKELMANN RK, MONTGOMERY H. FOX-FORDYCE DISEASE: A HISTOPATHOLOGIC AND HISTOCHEMICAL INVESTIGATION. ARCHIVES OF DERMATOLOGY. 1956; 74 :63 - 68.

WINKELMANN RK, KIERLAND RR, MONTGOMERY H. FOX-FORDYCE DISEASE IN THE MALE: REVIEW OF THE LTERATURE AND REPORT OF A CASE. ARCHIVES OF DERMATOLOGY. 1956; 74 :479 - 483.

WINKELMAN RK, HULTIN JV. MUCINOUS METAPLASIA IN NORMAL APOCRINE GLANDS. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY. 1958; 78 (3) :309 - 313.

WINTROBE MM. CLINICAL HEMATOLOGY. LEA AND FEBIGER. PHILADELPHIA. 1974.

WOODS G, VOGEL EH, CROAK J. HIDRADENITIS SUPPURATIVA AND PREGNANCY. OHIO STATE MEDICAL JOURNAL. 1972; 68 (9) :864 - 866.

WOOLLARD HH. THE CUTANEOUS GLANDS OF MAN. JOURNAL OF ANATOMY. 1930; 64 :415 - 421.

WYNN WILLIAMS D. THE SURGICAL TREATMENT OF SUPPURATIVE HIDRADENITIS. BRITISH JOURNAL OF PLASTIC SURGERY. 1953; 6 (3) :231 - 237.

ZELIGMAN I. TEMPORARY X-RAY EPILATION OF THERAPY OF CHRONIC AXILLARY HIDRADENITIS SUPPURATIVA. ARCHIVES OF DERMATOLOGY. 1965; 92 :690 - 694.

APPENDICES

APPENDIX 1

HIDRADENITIS SUPPURATIVA PROTOCOL

ADDRESSOGRAPH

DATE OF ATTENDANCE:

CONSULTANT:

SITES OF INVOLVEMENT

	RIGHT	LENGTH OF HISTORY	LEFT	LENGTH OF HISTORY
AXILLA	☐		☐	
GROIN	☐		☐	
THIGH	☐		☐	
PERINEUM/ PERIANAL	☐		☐	
GENITALIA	☐		☐	
INFRAMAMMARY	☐		☐	
OTHER SITE SPECIFY:	☐		☐	

PREVIOUS SURGICAL TREATMENT AT THE SITE(S)

DATE:_____ OPERATION:_____ SITE:_____

DATE:_____ OPERATION:_____ SITE:_____

DATE:_____ OPERATION:_____ SITE:_____

DATE:_____ OPERATION:_____ SITE:_____

DATE:_____ OPERATION:_____ SITE:_____

PREVIOUS MEDICAL TREATMENT ?

APPENDIX 1

ASSOCIATED CONDITIONS

	YES	NO	AGE OF ONSET	SITE
PREVIOUS HISTORY/ PRESENCE OF ACNE				
PREVIOUS HISTORY/ PRESENCE OF SEBACEOUS CYSTS				
PREVIOUS HISTORY/ PRESENCE OF PILONIDAL SINUS				

OCCUPATIONS DATES SPECIAL FACTORS

_____

_____

_____

_____

AGE AT MENARCHE: ☐☐ L.M.P. ☐☐☐☐☐☐

NO. OF PREGNANCIES ☐☐

CONTRACEPTIVE PILL: FROM: ☐☐☐☐☐ TO: ☐☐☐☐☐

☐☐☐☐☐ ☐☐☐☐☐

DAYS OF MENSTRUATION ☐☐ PATIENT'S HEIGHT AND WEIGHT

MENSTRUAL CYCLE (DAYS) ☐☐ ☐ ☐

ACTIVITY OF DISEASE IN RELATION TO PREGNANCY: _____

ACTIVITY OF DISEASE IN RELATION TO PERIODS: _____

FAMILY HISTORY:	YES	NO	STATE SITE AND/OR RELATIONSHIP
DIABETES	☐	☐	
HIDRADENITIS	☐	☐	

ALLERGIES: PLEASE NOTE

APPENDIX 1

MINOR DISEASE

CONSERVATIVE TREATMENT (Define)

LOCAL EXCISION (OPERATION NOTE)

MAJOR DISEASE

EXCISION (OPERATION NOTE)

HEALING BY SECONDARY INTENTION (SILASTIC FOAM DRESSING) ☐

SPLIT SKIN GRAFTING EXCISED SITE ☐

POSTOPERATIVE COMPLICATIONS:

APPENDIX 1

FURTHER TREATMENT NECESSARY

NOTE I.P.

O.P.

SITE: _____

TREATMENT:

_____

_____

_____

DATES:

OUTCOME:

APPENDIX 1

FOLLOW UP

CONDITION: _____

DATE	CONDITION OF SITE OF EXCISION	LIMB MOVEMENT	LIMB SWELLING	RECURRENCE AT SITE OF EXCISION	HIDRADENITIS AT NEW SITE	RETURN TO WORK/ ABSENCE FROM WORK

APPENDIX 2.

SITES OF INVOLVEMENT WITH HIDRADENITIS

PATIENTS' SEX	AXILLAE		GROINS + ADJACENT THIGH		OTHER SITES
	R	L	R	L	
FEMALE	-	+	-	-	-
FEMALE	-	-	+	+	LABIA MAJORA PERINEUM/PERIANAL
FEMALE	+	+	-	-	-
FEMALE	+	+	-	-	-
FEMALE	+	+	+	-	-
FEMALE	+	+	-	-	-
FEMALE	+	+	+	+	LABIA MAJORA PERINEUM
FEMALE	+	+	+	+	LABIA MAJORA PERINEUM
FEMALE	+	-	-	-	-
FEMALE	+	-	+	+	-
FEMALE	-	-	+	+	MONS PUBIS
FEMALE	+	+	-	-	MONS PUBIS
FEMALE	-	-	+	-	-
FEMALE	-	-	+	+	-
FEMALE	-	+	-	-	-
FEMALE	+	+	+	+	LABIA, MONS PUBIS PERINEUM
FEMALE	+	-	+	+	LABIA, MONS PUBIS PERINEUM
FEMALE	+	+	+	+	-
FEMALE	+	+	-	-	-
FEMALE	+	+	+	+	LABIA, MONS PUBIS PERINEUM
FEMALE	-	-	+	+	LABIA, MONS PUBIS PERINEUM
FEMALE	-	-	-	-	MONS PUBIS

APPENDIX 2.

PATIENTS' SEX	AXILLAE		GROINS + ADJACENT THIGH		OTHER SITES
	R	L	R	L	
FEMALE	+	+	+	+	-
FEMALE	-	+	-	-	-
FEMALE	-	+	-	-	-
FEMALE	+	+	+	+	-
FEMALE	+	+	+	+	LABIA, MONS PUBIS/ PERINEUM
FEMALE	-	-	+	+	-
FEMALE	+	-	-	-	-
FEMALE	+	+	-	-	-
FEMALE	-	-	+	+	LABIA, MONS PUBIS/ PERINEUM
FEMALE	-	-	-	-	SKIN OVER STERNUM
FEMALE	-	-	+	+	LABIA, MONS PUBIS/ PERINEUM
FEMALE	+	-	+	+	LABIA, MONS PUBIS/ PERINEUM INFRAMAMMARY FOLDS
FEMALE	+	+	+	+	LABIA, MONS PUBIS/ PERINEUM INFRAMAMMARY FOLDS
FEMALE	+	+	-	-	-
FEMALE	+	+	+	+	LABIA, MONS PUBIS/ PERINEUM
FEMALE	+	+	-	-	-
FEMALE	+	+	+	+	LABIA, MONS PUBIS/ PERINEUM
FEMALE	+	+	-	-	MONS PUBIS
FEMALE	+	+	-	-	SKIN OVER STERNUM
FEMALE	+	+	+	+	MONS PUBIS/PERINEUM
FEMALE	-	-	+	+	MONS PUBIS/PERINEUM
FEMALE	+	+	-	-	-
FEMALE	-	-	+	+	MONS PUBIS/PERINEUM
FEMALE	+	+	-	-	-
FEMALE	+	+	-	-	-
FEMALE	-	+	-	-	-
FEMALE	-	-	+	+	-

APPENDIX 2.

PATIENTS' SEX	AXILLAE		GROINS + ADJACENT THIGH		OTHER SITES
	R	L	R	L	
FEMALE	-	-	-	-	PERIANAL
FEMALE	+	+	-	-	-
FEMALE	+	+	-	-	-
FEMALE	+	-	-	-	-
FEMALE	+	-	-	-	-
FEMALE	+	+	-	-	-
FEMALE	+	+	-	-	-
FEMALE	+	+	-	-	-
FEMALE	+	+	-	-	-
FEMALE	+	-	-	-	-
FEMALE	+	+	-	-	-
MALE	+	+	-	-	-
MALE	+	-	-	-	-
MALE	+	+	+	+	-
MALE	-	-	+	+	PERINEUM/SCROTUM
MALE	+	+	+	+	PERINEUM/SCROTUM
MALE	+	+	+	+	PERINEUM/SCROTUM PERIANAL
MALE	+	+	+	+	PERINEUM/SCROTUM PERIANAL/SACRAL NAPE OF NECK
MALE	+	+	+	+	-
MALE	+	+	-	+	-
MALE	+	+	+	+	PERINEUM/SCROTUM PERIANAL/SACRAL
MALE	+	+	+	+	PERINEUM/SCROTUM SKIN OVER STERNUM
MALE	+	+	+	+	PERINEUM/SCROTUM
MALE	+	+	+	+	PERINEUM
MALE	+	+	+	+	PERINEUM/NATAL CLEFT/ PERIANAL
MALE	+	-	-	-	-

APPENDIX 3.

RESULTS OF GLUCOSE TOLERANCE TESTS PERFORMED ON HIDRADENITIS PATIENTS.

N = 27.

		PLASMA GLUCOSE MMOL/LITRE	URINE GLUCOSE
FEMALE	FASTING	4.9	-
	30 MIN	7.1	
	60 MIN	7.0	-
	90 MIN	5.5	
	120 MIN	6.1	-
FEMALE	FASTING	4.6	-
	30 MIN	9.2	
	60 MIN	7.0	-
	90 MIN	6.3	
	120 MIN	5.4	-
FEMALE	FASTING	5.2	-
	30 MIN	8.9	
	60 MIN	7.1	-
	90 MIN	6.1	
	120 MIN	4.9	-
FEMALE	FASTING	6.1	-
	30 MIN	11.9	
	60 MIN	11.3	-
	90 MIN	9.0	
	120 MIN	5.4	-
FEMALE	FASTING	3.8	-
	30 MIN	5.2	
	60 MIN	4.4	-
	90 MIN	5.6	
	120 MIN	4.2	-

APPENDIX 3.

RESULTS OF GLUCOSE TOLERANCE TESTS PERFORMED ON HIDRADENITIS PATIENTS.

		PLASMA GLUCOSE MMOL/LITRE	URINE GLUCOSE
FEMALE	FASTING	5.5	-
	30 MIN	9.4	
	60 MIN	11.6	-
	90 MIN	9.3	
	120 MIN	7.0	-
FEMALE	FASTING	4.9	-
	30 MIN	7.4	
	60 MIN	6.2	-
	90 MIN	6.0	
	120 MIN	6.1	-
FEMALE	FASTING	6.2	-
	30 MIN	9.1	
	60 MIN	8.0	-
	90 MIN	7.8	
	120 MIN	7.1	-
FEMALE	FASTING	4.7	-
	30 MIN	8.4	
	60 MIN	6.9	-
	90 MIN	5.0	
	120 MIN	5.0	-
FEMALE	FASTING	5.2	-
	30 MIN	8.2	
	60 MIN	6.8	-
	90 MIN	7.2	
	120 MIN	5.4	-

APPENDIX 3.

RESULTS OF GLUCOSE TOLERANCE TESTS PERFORMED ON HIDRADENITIS PATIENTS.

		PLASMA GLUCOSE MMOL/LITRE	URINE GLUCOSE
FEMALE	FASTING	4.8	-
	30 MIN	7.5	
	60 MIN	7.0	-
	90 MIN	5.9	
	120 MIN	4.3	-
FEMALE	FASTING	5.2	-
	30 MIN	9.0	
	60 MIN	8.7	-
	90 MIN	7.8	
	120 MIN	4.8	-
FEMALE	FASTING	4.8	-
	30 MIN	8.5	
	60 MIN	7.4	-
	90 MIN	6.6	
	120 MIN	6.5	-
FEMALE	FASTING	4.9	-
	30 MIN	11.9	
	60 MIN	13.9	+
	90 MIN	12.4	
	120 MIN	10.3	+
FEMALE	FASTING	4.9	-
	30 MIN	7.1	
	60 MIN	7.0	-
	90 MIN	5.5	
	120 MIN	6.1	-

APPENDIX 3.

RESULTS OF GLUCOSE TOLERANCE TESTS PERFORMED ON HIDRADENITIS PATIENTS.

		PLASMA GLUCOSE MMOL/LITRE	URINE GLUCOSE
FEMALE	FASTING	4.8	-
	30 MIN	6.7	
	60 MIN	6.6	-
	90 MIN	5.4	
	120 MIN	5.8	-
FEMALE	FASTING	5.5	-
	30 MIN	8.9	
	60 MIN	8.6	-
	90 MIN	5.9	
	120 MIN	4.0	-
FEMALE	FASTING	4.6	-
	30 MIN	9.2	
	60 MIN	7.0	-
	90 MIN	6.3	
	120 MIN	5.4	-
FEMALE	FASTING	5.6	-
	30 MIN	9.7	
	60 MIN	7.7	-
	90 MIN	7.3	
	120 MIN	5.8	-
FEMALE	FASTING	5.2	-
	30 MIN	8.9	
	60 MIN	7.1	-
	90 MIN	6.1	
	120 MIN	4.9	-

APPENDIX 3.

RESULTS OF GLUCOSE TOLERANCE TESTS PERFORMED ON HIDRADENITIS PATIENTS.

		PLASMA GLUCOSE MMOL/LITRE	URINE GLUCOSE
MALE	FASTING	4.9	-
	30 MIN	8.0	
	60 MIN	5.6	-
	90 MIN	5.2	
	120 MIN	4.8	-
MALE	FASTING	5.1	-
	30 MIN	8.9	
	60 MIN	6.3	-
	90 MIN	4.0	
	120 MIN	5.8	-
MALE	FASTING	4.9	-
	30 MIN	8.0	
	60 MIN	5.6	-
	90 MIN	5.2	
	120 MIN	4.8	-
MALE	FASTING	5.9	-
	30 MIN	10.3	
	60 MIN	9.3	-
	90 MIN	4.1	
	120 MIN	4.5	-
MALE	FASTING	5.3	-
	30 MIN	6.6	
	60 MIN	7.7	-
	90 MIN	6.4	
	120 MIN	6.3	-

APPENDIX 3.

RESULTS OF GLUCOSE TOLERANCE TESTS PERFORMED ON HIDRADENITIS PATIENTS.

		PLASMA GLUCOSE MMOL/LITRE	URINE GLUCOSE
MALE	FASTING	4.9	-
	30 MIN	8.0	
	60 MIN	7.3	-
	90 MIN	7.9	
	120 MIN	5.1	-
MALE	FASTING	5.1	-
	30 MIN	9.1	
	60 MIN	8.3	-
	90 MIN	5.9	
	120 MIN	3.7	-

APPENDIX 4.

THE NUMBERS, THE DIAMETERS AND SURFACE AREA OF THE APOCRINE GLANDS, IN ONE CM^2. OF AXILLARY SKIN TAKEN FROM HIDRADENITIS PATIENTS. (SLIDES 320)

	n = 21	n = 21	n = 32
SEX	NOS. OF GLANDS PER CM^2.	GLAND DIAMETER MM.	SURFACE AREA MM^2.
FEMALE	100	2.1	60.23
FEMALE	42	2.6	11.18
FEMALE	75	3.6	78.12
FEMALE	102	2.5	72.6
FEMALE	96	2.7	54.76
FEMALE	89	2.3	34.74
FEMALE	73	2.6	40.73
FEMALE	102	2.1	84.27
FEMALE	126	2.4	74.07
FEMALE	129	2.2	64.8
FEMALE	61	1.7	11.56
FEMALE	51	1.5	7.1
FEMALE	42	2.5	27.26
FEMALE	66	2.4	21.8
FEMALE			49.5
FEMALE			16.9
FEMALE			17.5
FEMALE			13.6
FEMALE			14.3
FEMALE			2.9 (FIBROSIS)
FEMALE			46.4
FEMALE			26.3
FEMALE			20.9

APPENDIX 4.

continued

SEX	NOS. OF GLANDS PER CM^2.	GLAND DIAMETER MM.	SURFACE AREA MM^2.
MALE	38	3.6	10.2
MALE	49	2.0	21.6
MALE	114	2.7	92.3
MALE	128	3.5	89.02
MALE	81	2.1	48.97
MALE	56	2.5	29.25
MALE	57	3.4	49
MALE			20.9
MALE			4.7 (FIBROSIS)

APPENDIX 5.

THE NUMBERS, THE DIAMETERS AND SURFACE AREA OF THE APOCRINE GLANDS IN ONE CM^2. OF AXILLARY SKIN, TAKEN FROM HYPERHIDROSIS PATIENTS.

(100 SLIDES)

	n = 8	n = 8	n = 10
SEX	NOS. OF GLANDS PER CM^2.	GLAND DIAMETER MM.	SURFACE AREA MM^2.
FEMALE	104	2.8	100.1
FEMALE	67	2.69	35.9
FEMALE	95	2.83	101.12
FEMALE			32.5
MALE	73	2.93	87.14
MALE	37	2.8	32.1
MALE	105	2.9	117.46
MALE	165	2.6	131.1
MALE	154	3.1	117.5
MALE			144.8

APPENDIX 6.

THE NUMBERS, THE DIAMETERS AND SURFACE AREA OF THE APOCRINE GLANDS IN ONE CM^2. OF AXILLARY SKIN TAKEN FROM CONTROL SUBJECTS.

(170 SLIDES)

	n = 10	n = 10	n = 17
SEX	NOS. OF GLANDS/ CM^2.	GLAND DIAMETER MM.	SURFACE AREA MM^2.
FEMALE	62	2.4	34
FEMALE	64	2.5	63.55
FEMALE	50	2.7	22.35
FEMALE	104	1.8	43.47
FEMALE	50	1.5	23.72
FEMALE	54	2.6	23.91
FEMALE	70	2.0	35.39
FEMALE	62	2.3	33.01
FEMALE	94	1.8	39.9
FEMALE			6.7
FEMALE			18.9
FEMALE			56.5
MALE	58	2.4	32.76
MALE			11.0
MALE			26.0
MALE			62.0
MALE			24.3

APPENDIX 7.

THE NUMBERS, THE DIAMETERS AND SURFACE AREA OF APOCRINE GLANDS IN ONE CM^2. SKIN TAKEN FROM OVER THE PUBIC TUBERCLE IN HIDRADENITIS PATIENTS. n = 18.

SEX	NOS. OF GLANDS/ CM^2.	GLAND DIAMETER MM.	SURFACE AREA MM^2.
FEMALE	0	0	0
FEMALE	0	0	0
FEMALE	0	0	0
FEMALE	0	0	0
FEMALE	18	1.6	4.5
FEMALE	20	1.4	6.9
FEMALE	0	0	0
FEMALE	0	0	0
FEMALE	0	0	0
FEMALE	1	0.9	-
FEMALE	0	0	0
FEMALE	0	0	0
FEMALE	5	1.5	1.1
FEMALE	5	1.5	1.2
MALE	0	0	0
MALE	0	0	0
MALE	0	0	0
MALE	0	0	0

APPENDIX 8.

THE NUMBERS, THE DIAMETERS AND SURFACE AREA OF APOCRINE GLANDS IN ONE CM^2. OF SKIN TAKEN FROM OVER THE PUBIC TUBERCLE IN NORMAL PATIENTS. n = 17.

SEX	NOS. OF GLANDS/ CM^2.	GLAND DIAMETER MM.	SURFACE AREA MM^2.
FEMALE	2	0.6	-
FEMALE	2	0.6	0.16
FEMALE	0	0	0
FEMALE	0	0	0
FEMALE	0	0	0
FEMALE	0	0	0
FEMALE	0	0	0
FEMALE	1	0.8	0.2
FEMALE	0	0	0
FEMALE	4	1.2	1.06
MALE	0	0	0
MALE	0	0	0
MALE	0	0	0
MALE	0	0	0
MALE	0	0	0
MALE	0	0	0
MALE	10	1.4	2.97